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CONTRIBUTORS TO THIS NUMBER

PERCY B DAVIDSON M D Assistant in Medicine Harvard Medical School, Assistant Thorndike Memorial Laboratory Boston City Hospital Gastro-enterologist, Beth Israel Hospital

EDWARD S EMERY JR. M D Assistant in Medicine Harvard Medical School Junior Associate, Peter Bent Brigham Hospital

RAPHAEL ISAACS M D Instructor in Medicine Harvard Medical School, Assistant Physician Colus P Huntington Memorial Hospital of Harvard University

ELLIOTT P JOSLIN M D Clinical Professor of Medicine Harvard Medical School, Consulting Physician Boston City Hospital, Physician to New England Deaconess Hospital.

EVERETT D KIEFER, Boston.

CHARLES H LAWRENCE, M D Chief of Service Clinic for Endocrine Research Evans Memorial Hospital Lecturer in Medicine Boston University Medical School

ROGER I LEE, M D., Member of the Associate Staff of the New England Deaconess Hospital

SAMUEL A. LEVINE, M D., Associate in Medicine Peter Bent Brigham Hospital Instructor in Medicine Harvard Medical School

EDWIN A. LOCKE, M D Clinical Professor of Medicine, Harvard Medical School Visiting Physician Boston City Hospital.

CHARLES W. MCCLURE, M D Gastro-intestinal Research Worker and Gastro-enterologist, Evans Memorial Hospital

JOHN LOVETT MORSE M D Professor of Pediatrics Eminent Harvard Medical School Consulting Physician to the Children's Infants and Floating Hospitals.

H. ARCHIBALD NISSEN M D Junior Visiting Physician Boston City Hospital Assistant Visiting Physician, Robert Breck Brigham Hospital Alumni Instructor in Medicine Harvard Medical School

JAMES P O'HARE M D Associate in Medicine Peter Bent Brigham Hospital

JOSEPH H PRATT M D Formerly of the Massachusetts General Hospital

WILLIAM H ROBEY M D Assistant Professor of Medicine in the Harvard Medical School Visiting Physician to the Boston City Hospital Consulting Physician to the Milton Hospital

HOWARD F ROOT M D Assistant Physician, New England Deaconess Hospital

HOWARD B SPRAGUE M D Research Resident, Massachusetts General Hospital and Dalton Fellow Massachusetts General Hospital

HENRY R. VIETS M D Assistant Neurologist Massachusetts General Hospital Instructor in Neurology Harvard Medical School.

PAUL D WHITE M D Associate in Medicine Massachusetts General Hospital Instructor in Medicine Harvard Medical School

PRISCILLA WHITE, M D Boston.

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THE MEDICAL CLINICS OF NORTH AMERICA

Volume 8

No 6

CONTRIBUTION BY DR JOHN LOVETT MORSE

CONSULTING PHYSICIAN TO THE CHILDREN'S, INFANTS', AND
FLOATING HOSPITALS

CONGENITAL HEART DISEASE

I FIND from my records that I have made the diagnosis of congenital heart disease in 114 cases seen in private and consultation practice. On looking over the records there seems to be some doubt as to the accuracy of the diagnosis in a number of cases. It was certainly correct, however, in at least 100 of them. The number of cases of any sort represents, therefore, the percentage of such cases. I shall not attempt to analyze these cases in detail or to take up the individual symptoms separately. Certain points are, however, of considerable interest, and some of them are not in agreement with the commonly accepted views.

It is well known that congenital heart disease is often associated with other congenital malformations and that Mongolian idiocy is not infrequently accompanied by cardiac malformations. In this series there were 6 Mongolian idiots and 5 other feeble-minded children, that is, there were cerebral defects in more than 10 per cent of the cases. One baby had atresia of the esophagus and malformation of the hands, another, malformation of the sternum and undescended testicles, and another had club-feet. It was only once in this series that there were 2 cases of congenital heart disease in the same family.

Symptomatology — This series shows that the classical statements that symptoms may or may not be present at birth, that

cyanosis and dyspnea are the most striking symptoms, that clubbing of the fingers and toes seldom develops before the end of the first year, and that death may occur suddenly, without there having been any previous symptoms, are true. They emphasize the frequency of "attacks" or "spells" of various sorts. Three had attacks of dyspnea and cyanosis without apparent cause, and one of these children not infrequently became unconscious and had convulsions during the attacks. Two others had convulsive attacks. One had attacks of apnea in which it became blue and limp. Another had spells in which it was sometimes white and sometimes blue. Another had attacks of exhaustion and still another spells of twitching.

One of the most striking things in this series is the frequency with which there were marked symptoms of cardiac disease without any, or with only a very slight, murmur. In 3 instances there was no murmur. In 1 of these, which was first seen when it was a week old, there was general cyanosis which became very deep when the baby cried. The heart was normal in every way. The lungs were expanded and there were no evidences of enlargement of the thymus. It was seen again when five months old. It was still slightly cyanotic and became deeply so whenever it exercised or cried. The heart was, as before, perfectly normal. Another baby, which was seen when nine days old, was cyanotic at birth and very cyanotic at the time. The heart was perfectly normal. There were no evidences of atelectasis. It died when four weeks old, never having developed a murmur. Another baby, which was seen when it was four days old, was not cyanotic, but was in very poor general condition, moaning and twitching. The heart was normal in every way and the lungs expanded. There was no evidence of infection or hemorrhage. It died suddenly twenty-four hours later. The autopsy showed a patent ductus arteriosus.

It is possible that murmurs might have been found later in these babies if they had lived or had been seen when they were older. In 2 other instances this happened. In one, in whom there was no murmur at birth, symptoms and a murmur developed when the baby was two months old. In another in-

stance no murmur was heard until the baby was eight months old, although it was repeatedly and carefully examined. This murmur was much more marked at a year, and was quite loud at two and two-thirds years, when the child was stronger and better. The murmur was still present, the heart was enlarged, and there was slight cyanosis at six and a half years. In a hospital case, which I reported some years ago that had the most marked signs of congenital heart disease, no murmur was heard until just before death, at about nine years. This murmur was due moreover to an acute endocarditis.

In 4 other babies who showed very marked evidences of cardiac disease there was only a slight murmur. In one, seen at two and a half months who was blue at birth and afterward, was always short of breath and who had convulsive attacks, a slight murmur could sometimes be heard at others, none at all. In another, seen at eighteen months, cyanosis began at three months and persisted. The baby was short of breath. There was clubbing of the fingers and toes. The murmur, however, was very slight. In another baby, seen at two weeks who had been blue at birth and since, the color was leaden, but there was only a slight systolic murmur at the apex. Another, aged eighteen months, was markedly blue from birth. There was clubbing of the toes. The cardiac area was normal however, and there was only a slight systolic murmur in the mitral area. It is probable that in most of these cases in which there are marked symptoms of cardiac disease and no or a very slight murmur, the lesion is either a large defect in the septum or a transposition of the vessels.

Prognosis—It is very striking in how many cases there were loud murmurs, unquestionably congenital in origin, in which there were no symptoms. There were 12 such cases, in all of which the murmur was either present at birth or discovered during the first few months of life. There are too many of these to take them all up in detail. It is possible that some of them who were only from five to eight years old when last seen, may have developed symptoms later. Incidentally, one of these children, a girl of six, had a complete situs transversus. I will,

therefore, mention only a few of them in detail. One of these, a boy whom I saw first when he was five years old, had been in the charge of the late Dr T M Rotch up to that time, who had found a murmur in his heart soon after birth, and had said that he had congenital heart disease. When I saw him the heart was slightly enlarged to the right. The area was otherwise normal. The action was regular. The first sound was loud and clear. It was followed by a loud, rough, blowing murmur, which was loudest at the base. It was audible in the neck and could be heard over the whole chest. The two second sounds in the aortic and pulmonic areas were of about the same intensity. He had never had any cardiac symptoms. He is now twenty-seven years old, his heart is not enlarged, the murmur is the same. It can be heard very distinctly over the whole chest, back and front. He has never had any symptoms referable to the heart. He has played football, boxed, and taken the Reserve Officer's Training Course in college.

Another patient, whom I did not see until she was twenty-three years old, had considerable enlargement of the heart to the left. The first sound was strong, except at the pulmonic area, where it was replaced by a loud, rough, blowing murmur, which was transmitted upward and into the back. This murmur could also be heard over the rest of the heart, but much more feebly. The two second sounds were of about the same intensity. The congenital heart lesion was discovered when she was two years old. She had never had any symptoms referable to the heart, but within the past few months had developed pulmonary tuberculosis. Death occurred four months later from the tuberculosis. The autopsy showed a narrowing of the pulmonary artery.

In another instance I discovered a cardiac murmur during a routine examination of a baby nineteen months old. As the baby had had no symptoms, I thought that it might be functional. When he was five years old the heart was slightly enlarged to the right and the first sound over the whole precordia was followed by a loud, harsh murmur, which was heard in the neck and back. There was a thrill in the suprasternal space. The

second pulmonic sound was accentuated. A probable diagnosis of patent ductus arteriosus was made. He had had no symptoms at that time. He is now seventeen years old. There has been no change in the physical signs in the heart. He has done and still does everything that any boy does—plays football, climbs mountains, and leads a normal life. He has never had any symptoms referable to the heart.

Another boy, thirteen years old when seen, was the son of a physician. The cardiac lesion was discovered at birth. He had never had any symptoms whatever referable to the heart. The cardiac area was normal. The action was regular. The first sound over the whole precordia was replaced by a loud, rough murmur. It was also audible over the whole chest. It was loudest in the pulmonic area. There was no second pulmonic sound.

It is evident from these cases that the prognosis in congenital heart disease does not depend so much on the intensity or location of the murmur as it does on the presence or absence of other symptoms. It is evident also from these cases that a child with a congenital cardiac lesion may reach adult life without the development of any symptoms. It is very probable that it may never have any trouble from its heart, lead just as active a life as other people, and live as long as if it did not have it.

Another striking thing brought out by these cases is how long a child may live and how much it may accomplish, even when the congenital heart lesion is accompanied by marked symptoms. For example, a girl, first seen when three years old, was known to have had heart disease since early infancy. At that time the heart was enlarged both to the right and to the left. The sounds were strong, but the first sound over the whole precordia was continued into a loud, blowing murmur, loudest in the neighborhood of the apex. The second sound at the aortic area was replaced by a high-pitched, blowing murmur, which was heard in the pulmonic area and which was transmitted down the right side of the sternum and a little to the left. The second pulmonic sound was considerably accentuated. There

first two pregnancies resulted in miscarriages at eight months. The third baby was carried to full term and was normal and vigorous. She was no more cyanotic during pregnancy than at other times and was not in danger during her deliveries. She was everywhere markedly cyanotic. There was no clubbing of the fingers. The liver and spleen were normal. The red blood-count was usually normal but once was as high as 5 632 - 000. The cardiac action was regular. The rate was 80. The area was normal. There was a soft blowing murmur at the pulmonic area and occasionally at the lower end of the sternum. The second pulmonic sound was slightly accentuated.

There are several other cases of this sort in the series. It is also very striking how many children with congenital heart lesions survive other diseases even those of the lungs and whooping-cough. There are many examples of this sort in this series.

The question always comes up as to whether recovery from congenital heart disease is possible. It must be remembered in this connection that congenital heart disease, so-called, is really not a disease the conditions which are described under this name being really abnormalities or malformations of the heart and great vessels. The causes of congenital heart disease may be divided into three classes, persistence of fetal conditions, interference with normal development, and fetal endocarditis. The only important anomalies resulting from the persistence of fetal conditions are patency of the foramen ovale and of the ductus arteriosus. These may be only lesions or may be the result of other cardiac lesions. The most common abnormalities resulting from interference with normal development are defects in the septa more often in the ventricular than in the auricular and stenosis or atresia of the orifices, most commonly of the pulmonary. Malformations of the great vessels are also not uncommon. Fetal endocarditis almost always occurs on the right side and usually effects the pulmonary valves.

Combinations of lesions, as the result of a combination of the causes just mentioned are very common. Inflammatory lesions and anomalies which result in narrowing of the orifices,

and hence in a local increase of intracardiac pressure, prevent the normal development of the heart, especially of the septa, which fail to close, because of the necessity for a compensatory circulation. For the same reason the foramen ovale and the ductus arteriosus often continue open after birth.

It is possible that a persistent fetal condition may be finally overcome. It is not likely that any lesions due to interference with normal development can be corrected or overcome by growth. When it is thought that recovery takes place, the chances are that the diagnosis was wrong. Nevertheless, there were 2 cases in this series in which the diagnosis seemed certain at the time, in whom the signs disappeared, and who are now well at the ages of fourteen and twenty-five years, respectively. In one the murmur was discovered at eight months during the course of a routine examination. He had had no symptoms pointing to the heart except that he was a little blue during the first ten days after birth. He was in good general condition and his color was good. The cardiac area was normal. The action was regular. There was a systolic murmur at the mitral area and apex, which was loud and musical, and was transmitted into the axilla and back. The same murmur was heard feebly at the base. The second pulmonic sound was not accentuated. There was no venous hum in the neck. The murmur persisted until he was about three years old. He had no symptoms. The murmur was gone and the heart was normal in every way when he was three and a half years old. It is still normal at fourteen years.

In another case a systolic murmur was heard over the whole precordia when the baby was two months old, the first time that he was examined. It followed the first sound and was loudest at the base. This murmur was also audible in the back. The second pulmonic sound was not accentuated. He was small and thin, but of good color. He never had any symptoms referable to his heart. The murmur had disappeared when he was six months old and did not return. He is now twenty-five years old and has a normal heart.

Diagnosis.—The general principles of the differential diag-

nosis between congenital heart disease and other cardiac conditions are easy. There are certain main points which are of importance in distinguishing between congenital and acquired heart disease. The mere fact that there are signs of cardiac disease in infancy and early childhood is strong evidence in favor of a congenital lesion. When there is no history of any disease in the past likely to cause cardiac disease, the evidence in favor of a congenital lesion is still stronger. Cyanosis and clubbing of the extremities without heart murmurs or other evidences of disease sufficient to account for them, and cyanosis and clubbing of the extremities without signs of venous congestion in other organs, count strongly in favor of a congenital against an acquired lesion. So also do loud murmurs without enlargement of the heart. Diastolic murmurs are practically never congenital. A combination of physical signs not consistent with those usually found in the various forms of acquired cardiac disease is strongly suggestive of a congenital lesion. The presence of other congenital abnormalities favors the diagnosis of congenital disease, and the presence of the characteristic signs of the various congenital lesions makes the diagnosis almost positive.

The diagnosis between the murmurs due to congenital heart lesions and cardiopulmonary murmurs is not difficult. The cardiopulmonary murmurs vary with position or respiration, and with them there is no enlargement of the heart or other symptoms of cardiac disease. Another murmur, which is frequently heard in infancy over and above the manubrium and which is probably due to pressure on the innominate veins, ought not to be confused with the murmur of a congenital lesion, because it is increased by extension of the head and is not associated with any other signs of cardiac disease. A systolic murmur is very often heard in the pulmonic area throughout childhood. The cause of this murmur is not certainly known. It is, however, soft and not associated with a thrill, enlargement of the right side of the heart or weakening of the second pulmonic sound, one or more of which signs is almost always present when a murmur in the pulmonic area is due to a

congenital lesion. Moreover, there are never any other evidences of cardiac disease, such as are usually present with a congenital lesion. The so-called functional murmurs, which may be heard at any of the orifices as the result of lowered muscular and nervous tone, are usually not present in infancy, but occur later, when most of the children with congenital lesions are already dead. These murmurs are always soft and are not associated with other evidences of cardiac disease, unless possibly slight enlargement of the heart. Their distribution, moreover, is not that of congenital, but of acquired, lesions.

Nevertheless, it is sometimes very difficult to distinguish between congenital heart disease and certain other conditions. I have made a number of mistakes of which I know and probably others of which I do not know. Some of these cases are instructive enough to mention in detail.

A baby, which was seen when it was thirty-two hours old, was delivered by cesarean section at term. It cried hard at once. There was considerable mucus in the throat. Three hours later it became cyanotic and began to have a whining cry. The cyanosis continued intermittently up to three hours before it was seen. The whining cry continued constantly. It took a short inspiration, which was followed by a long expiration with the cry. At the beginning of the cyanosis the temperature was about 1 degree below normal. Since then it had been kept 1 degree or so above normal with heaters. There had been no twitching and no other nervous symptoms. It was a little pale, but not cyanotic. There were no evidences of a cerebral hemorrhage. The mouth and throat were normal. The heart was normal. The baby took a short inspiration. With it there was marked retraction of the epigastrium, but very little motion of the chest. There was then a rather longer expiration, with a whining cry. The air did not enter the backs well, especially on the right. A very few fine râles were heard on the left. There was no change in the percussion note over the lungs. The liver was 1 cm. below the costal border. The spleen was not palpable. I made an almost positive diagnosis of atelectasis of the lungs. The baby died a few hours later. The autopsy showed a very

large ductus arteriosus, the ductus being larger than either the aortic or the pulmonary artery. As a result there was a tremendous congestion of the lungs, which gave the respiratory symptoms and accounted for the conditions found in the lungs. Death resulted from congestion in the lungs, although the primary lesion was in the heart.

A baby that was seen at eleven weeks had a history of cyanosis during the first two days of life. After this the cyanosis gradually disappeared and was replaced by pallor. Two weeks before she was seen she began to have spells of cyanosis which had been worse during the last three days and nights. She had cried a great deal the last three nights. During this time she had not been doing well with her food. She had vomited off and on and had had several green, undigested movements each day. During the night before she was seen she had been cyanotic and the pulse and breathing had been poor. Under stimulation she had improved somewhat. When seen she was markedly pale and there was a distinct tinge of cyanosis which was especially marked in the lips and nails. She was in fair general condition. The general examination was negative. The stools were small, watery green, and contained curds and mucus. A positive diagnosis of congenital heart disease was made, and the disturbance of digestion was thought to be a side issue. Under treatment she quickly improved and with a change in the diet all the symptoms disappeared. She never had any further evidences of cardiac disease. In this instance the cyanosis was probably simply an evidence of poor circulation resulting from the indigestion. It is possible that it may have been due in part to toxemia from intestinal absorption.

Another baby that was born about one month premature was seen when ten days old. It was feeble and there was considerable difficulty in keeping its temperature up to normal in the morning, even with heaters. As it was doing fairly well, the nurse thought two days before, that it might be treated as a normal, full-term baby. Consequently she stopped the heaters and bathed the baby each morning. The baby had taken the breast fairly well up to the day before when it began

to refuse it. It was kept at the breast for long periods, shaken up, and thoroughly tired out. The morning of the day it was seen it collapsed.

It was small and poorly nourished. The color was fair. There was a systolic murmur over the whole precordia, loudest about the middle. It was heard also in the back. It was not very loud. The cardiac action was regular and the area normal. The lungs were normal. In this instance it was thought that the cardiac murmur might be due either to a congenital heart lesion or to a general disturbance of the nutrition and feebleness. The murmur gradually disappeared as the baby grew stronger, and there were no signs of a cardiac disease when it was seen at three and three-quarter years. It had had no symptoms.

I have made the mistake several times of mistaking a murmur in the heart of a young, feeble baby, resulting from poor general condition, for a congenital heart murmur. The diagnosis is practically impossible in many instances when the baby is first seen. Time alone will reveal the cause of the murmur. It is well to remember, however, that when a young baby is feeble or somewhat anemic, cardiac murmurs may be functional instead of organic. Under such conditions it is not wise, therefore, to make a positive diagnosis of a congenital lesion in the beginning.

It is possible that a murmur at the base of the heart in a young baby may be due to the pressure of an enlarged thymus gland. In my experience, however, this is a very uncommon occurrence. Other symptoms of pressure of the thymus, such as difficulty with the respiration, are much more likely to occur. Even when there is cyanosis from pressure of the thymus it is not likely to be accompanied by a cardiac murmur because the pressure is usually on veins rather than on arteries. A murmur due to pressure of the thymus is also likely to be much softer and more localized than the murmur of congenital heart disease.

When there is no question as to the accuracy of the diagnosis of congenital heart disease it is, nevertheless, usually very difficult, if not impossible, to make a positive diagnosis of the exact

abnormality, partly because several lesions may give the same signs, partly because of the frequency of combined lesions, and partly because of the occasional presence of most unusual anomalies. Many of the points which are often emphasized in the diagnosis of special lesions are of no practical value. It is not reasonable, for example, to believe that when the ductus arteriosus is patent, even if it is enlarged, it will be possible to percuss out a tube, less than an inch long and not much larger than a slate pencil, deep down in the neck under the manubrium. The Roentgen ray, which theoretically ought to be of considerable value in the diagnosis of special lesions, is practically of little assistance, even in the hands of an expert. Fortunately, the diagnosis of the exact lesion in these cases is not of great importance in either prognosis or treatment. The signs of certain lesions are, however, fairly constant and characteristic.

Murmurs are often lacking in cases of patency of the foramen ovale. When present, they are usually blowing and are loudest near the base of the heart. In one instance, in which the diagnosis of patency of the foramen ovale was proved at autopsy, a systolic murmur over the whole precordia was discovered soon after birth. The baby was not markedly blue. When seen at two months he was small and thin, but his color was fair. The cardiac area was normal. The first sound was continued over the whole precordia into a soft, blowing murmur. It was also audible in the back. The second sound was not very loud. It was louder at the pulmonic area than elsewhere.

A murmur, loudest at the base, accompanied by a thrill at the base and in the suprasternal notch, and with little or no enlargement of the cardiac dulness, points to patency of the ductus arteriosus. The following case is an example. A little girl first showed cyanosis at three years. This continued, and dyspnea on exertion developed. When seen at ten years she was well developed and nourished. There was slight general cyanosis, becoming fairly marked in the lips, cheeks, and nails. The right border of the cardiac dulness was 3 cm. to the right and the left 8 cm. to the left of the median line. The upper border was at the upper border of the third rib. The cardiac

impulse was rather feeble. There was slight dulness under the manubrium. A systolic thrill was palpable in the suprasternal space. The first sound over the whole precordia was continued into a blowing murmur. This was very marked under the manubrium, and a little louder to the right than to the left. It was relatively slight at the apex. It was heard distinctly in the neck and over the whole back, but louder in the upper than in the lower back. The second sounds were distinct at the base, being louder at the pulmonic than at the aortic area. The liver and spleen were palpable. There was slight clubbing of the fingers and toes.

A loud murmur, most marked at the center of the heart dulness, not accompanied by a thrill, and without enlargement of the cardiac area, points toward a defect in the ventricular septum. This case is an example. A boy thirteen months old was a little blue at birth and had continued to be so. The cyanosis was very marked when he cried. He had attacks in which the breathing was very bad and in which he was much distressed. He was small and thin. There was marked cyanosis of the lips, fingers and toes, and a little of the face. There was slight clubbing of the fingers and toes. The right border of the cardiac dulness was $2\frac{1}{2}$ cm. to the right and the left border $5\frac{1}{2}$ cm. to the left of the median line. The upper border was in the second space. The action was regular. There was a loud systolic murmur over the whole precordia, loudest in the fourth left space. The first sound was feeble. The second sound was everywhere distinct. There was no enlargement of the liver and spleen.

In another baby the murmur was discovered when he was three months old. He had had no symptoms of heart disease. The murmur increased rapidly in intensity, and a thrill developed. He showed no symptoms except a little trouble in nursing. When seen at six months his color was fair and he was in good general condition. There was a slight thrill at the apex and over the middle of the heart. The first sound over the whole precordia was replaced by a loud, long, rough murmur, which was loudest over the center of the heart and was trans-

mitted through the apex into the axilla and back. There was no second sound at the base. Elsewhere it was heard indistinctly. The right border of the cardiac dullness was 2 cm. to the right and the left border $6\frac{1}{2}$ cm. to the left of the median line. There was no clubbing of the extremities and no cyanosis.

A murmur, loudest at the base, accompanied by a thrill and enlargement of the heart to the right, with a feeble second pulmonic sound and cyanosis, points to a narrowing of the pulmonary orifice. A baby, seen first when it was five months old, was blue at birth and continued so. It was short of breath if it cried. It was poorly developed and nourished. There was moderate general cyanosis, with marked cyanosis of the face, hands, and feet. The right border of the cardiac dullness was 2 cm. to the right and the left border 6 cm. to the left of the median line. The action was regular. The first sound at the base was replaced by a soft blowing murmur, which was audible over the whole chest. The second pulmonic sound was much feebler than the second aortic. There was no thrill. In another baby, seen at five months, blueness developed about two hours after birth. The cyanosis continued, but varied in intensity. It was generally a little dusky, while the lips and nails were blue. The right border of the heart was 2 and the left border 6 cm. to the right and left of the median line, respectively. The action was regular. The first sound over the whole precordia was continued into a long, blowing murmur, loudest at the base. It was also heard in the back. The second pulmonic sound was much diminished. There was a very slight thrill in the pulmonic area. There was no enlargement of the heart in either of these cases. If the diagnosis of pulmonary stenosis was correct, however, enlargement of the heart almost certainly developed later.

If there is patency of the ductus arteriosus in addition to stenosis of the pulmonary orifice, theoretically, the location of the murmur is the same as in pure stenosis of the pulmonary orifice, while the second pulmonic sound is normal or increased in intensity as the result of the flow of blood through the ductus arteriosus. A thrill may also be present in the suprasternal

notch The physical signs in this case correspond to those of pulmonary stenosis and patency of the ductus arteriosus A heart murmur was discovered at ten months during a routine examination He had had no evidence of cardiac trouble at that time I saw him when he was four years old His color was good except when he cried Then there was a slight cyanotic tinge in the cheeks The cardiac impulse was in the fifth space in the nipple line, $6\frac{1}{2}$ cm to the left of the median line The right border of dulness was 3 cm to the right and the left $6\frac{1}{2}$ cm to the left of the median line There was a loud, rough, systolic murmur over the whole precordia This was loudest in the second left space It was transmitted upward into the neck and also into the axilla It was distinctly audible in the back There was a very distinct thrill in the second left space The second pulmonic sound was accentuated There was no clubbing of the extremities The liver and spleen were normal

Diastolic and double murmurs are very unusual in congenital heart disease Their presence always throws doubt on the diagnosis In one instance, however, the baby was blue at birth and continued to be blue The cyanosis was at times very marked She was unable to run or play because of dyspnea When seen first, at seven years, there was slight cyanosis of the lips and extremities, which became very marked when she cried The right border of the cardiac dulness was $3\frac{1}{2}$ cm to the right and the left $6\frac{1}{2}$ cm to the left of the median line The upper border was at the upper border of the third rib There was no thrill The action was regular There was a systolic murmur over the whole precordia, loudest at the base There was also a diastolic murmur at the mitral area In places there was a continuous murmur throughout the whole cardiac cycle It was audible over the whole chest There was no enlargement of the liver and spleen There was very little clubbing of the fingers and toes It is utterly impossible with signs like these to make even a guess at the location of the cardiac lesion

Murmurs at the aortic area are also extremely rare in congenital heart disease A little girl had a severe attack of cyanosis about a week after birth There had been no return, but

she had always been short of breath on exertion and had had a cough on running. She was seen when three years old. She was well developed and nourished. Her color was good. There was no clubbing of the fingers. The heart area was normal, but over the upper part of the sternum and in the first right space, where it was most marked, there was a rough, systolic murmur, which was transmitted upward into the neck. The second sound was normal in both the aortic and pulmonary areas. There was no thrill. In this instance, also, it is impossible to more than guess at the pathologic condition. Some abnormality of the vessels seems more probable, however, than an aortic stenosis.

Fortunately, the diagnosis of the exact lesion in congenital heart disease is not of great importance in either prognosis or treatment. In a general way patency of the foramen ovale diminishes the expectancy of life but little, and simple defects of the ventricular septum are not incompatible with long life; neither are certain combined lesions in which the lesions to a certain extent neutralize each other. The determination of the lesion is so difficult however that clinically little reliance can be placed on the diagnosis of the lesion in prognosis, this depending on the general condition and character of the circulation in the individual patient rather than on special symptoms and signs.

Treatment—There is of course no curative treatment. There is nothing which will either diminish the deformities or favor the closure of abnormal openings. The treatment must, therefore, be hygienic and symptomatic. Breast feeding, maintenance of the body temperature and the prevention of infection are of the most importance in the beginning. Infections of the respiratory tract are very dangerous and must be especially guarded against. A comparatively warm, dry climate is, therefore, most suitable. Overexertion and excitement must be avoided in older children. Insufficiency of the heart muscle calls for digitalis as it does in acquired heart disease. Sudden severe symptoms are to be treated as in acquired heart disease by nitroglycerin and the quick cardiac stimulants, such as strychnin and ammonia. The sudden attacks of suffocation and the convulsions are best avoided by the use of bromid.

CLINIC OF DR EDWIN A LOCKE

BOSTON CITY HOSPITAL

SPONTANEOUS RUPTURE OF THE HEART

WE are to discuss today a somewhat rare but very important and interesting condition. Apart from the actual penetrating wounds of the chest with puncture of the heart, ruptures of the walls of the heart are usually classed as traumatic or spontaneous. The former type, comprising a very small group of approximately 100 reported cases, is the result of external injury, such as violent compression of the chest from any cause, direct blow over the precordia, and fall from a height sufficient to cause fatal injury. Traumatic rupture of the heart often occurs with only slight or no external evidence of injury. Rupture of the precordia as well as of the heart muscle is by no means uncommon in these cases.

In contrast to this type of rupture following external trauma is a much more common form, in which sudden death results from giving way of the heart muscle, which is in no way dependent on external injury, and known as "spontaneous rupture of the heart." The 2 following cases are excellent examples of this condition.

Case I Arteriosclerosis, Right Hemiplegia, Complete Motor Aphasia, Lymphangitis of Legs, Sudden Death from Rupture of Right Ventricle—A married woman aged fifty-one. No history could be obtained because of the patient's aphasia.

Physical Examination—Partial paralysis of right side of face, lines and furrows not so prominent as on other side. Tongue deviates toward the right. Patient appears to understand perfectly all that is said to her, but is utterly unable to articulate. She walks with the aid of the nurse.

Heart Apex in fifth space 0.5 cm within nipple line, right border just within right sternal border, action slightly irregular, no murmurs heard, aortic second sound increased

Extremities Right arm contracted and held across breast, fingers strongly flexed, deep reflexes increased No edema or tenderness of legs Knee-jerk increased and Babinski present on right

Examination otherwise normal

The patient remained in the hospital for nearly two years, during which time there was increasing helplessness At times the heart action was very weak and irregular During the last few months of her life she had several severe attacks of lymphangitis in both legs, and finally became bedridden

At 4.30 A. M. one morning, after having slept nearly all night as usual, she indicated to the nurse that she wished to have a movement of the bowels The nurse reported that she found the patient very cyanotic, breathing with great difficulty, and evidently in great distress if not actual pain Death followed within a few minutes

*Autopsy, nine hours postmortem Abstract of report Anatomic diagnosis**

Chronic adhesive pleuritis

Hemopericardium

Rupture of the heart (right ventricle)

Hypertrophy and dilatation of the heart

Acute vegetative endocarditis (mitral)

Fatty infiltration of the heart

Chronic passive congestion of the lungs

Adhesions of the sigmoid flexure

Chronic passive congestion of the liver

Chronic nephritis

Multiple infarcts of the kidneys

Edema of the brain

Degeneration of the crossed and direct pyramidal tracts (right)

Pleural cavities Both present numerous old fibrous adhesions, the right completely adherent to the lung and diaphragm

Pericardial cavity. Contains about 75 c c of dark, bloody fluid

Heart. Weight, 450 gm ; length, 18 cm , breadth, 13 cm , epicardial fat abundant The front wall, at a point 3.5 cm from the apex and 1 cm to the right of the coronary artery, presents a ragged tear 2 cm in length, the edges fresh and opening into the right ventricle The auricles distended with currant jelly clot. Upon section, the myocardium of the left ventricle beefy red, of the right, extensively infiltrated with fat, notably in the region of the apex, where the epicardial fat apparently extends through to the papillary muscles Left auricle dilated Wall of left ventricle 1.3, of right 0.6 cm , in thickness Mitral valve 9, aortic valve 7.2, pulmonary valve 7, tricuspid valve 11.5 cm in circumference The mitral valve presents slight general thickening and puckering of the curtains, notably of the posterior, with shortening and thickening of the chordæ tendinæ, along the line of apposition of the curtains are multiple granular elevations, for the most part about 1 mm in diameter, some of them pink, others yellowish white. The anterior curtain presents a collection of these elevations in the form of a somewhat sessile outgrowth about 5 mm in elevation Some of the nodules on the posterior curtain are partially calcified The papillary muscles of this valve are yellowish white at their tips Left ventricle slightly dilated Coronary arteries present a slight degree of sclerosis

Aorta Upon section presents numerous slightly elevated disk-like plaques mostly 1 cm in diameter, many of them calcareous

Case II Advanced Arteriosclerosis; Senile Dementia; Fracture of Left Humerus; Sudden Unconsciousness Due to Rupture of Left Ventricle, Death Eight Hours Later—Man, aged eighty-one, an inmate of the Boston Almshouse, a wheelwright by trade, admitted to hospital because of injury to arm resulting from a fall from his chair Patient moderately demented and no history obtained

Physical Examination—General appearance of advanced

senility Pupils equal, react sluggishly to light, no reaction to distance, vision poor, right eye shows opacity of lens Tongue protrudes straight in median line, heavily coated, slightly tremulous Pulse irregular and of poor volume and tension Marked sclerosis of radial and brachial arteries

Heart Dulness extends from the nipple line on the left to right sternal border, apex-beat in fifth space, action slightly irregular, sounds rather weak A loud blowing systolic murmur is heard at the apex, transmitted into the axilla A systolic murmur of similar character is heard at the base, though of less intensity, the latter is audible along both sternal borders and in the right nipple line at the level of the third rib

Evidence of fracture of left humerus Otherwise the examination shows nothing strikingly abnormal

The fracture healed promptly and the general condition showed slow improvement Three months after entrance to the institution the following note is given in the record

"Yesterday the patient was out-of-doors, feeling as well as ever Last night he was taken to the bath-room and given a cleansing bath He had been dried, and was almost ready to be taken back to bed, when he suddenly fell from his chair The respiration was very shallow and difficult, skin cyanotic, and pulse barely to be felt Auscultation of the heart revealed only feeble sounds, somewhat rapid and irregular By means of stimulants and occasional artificial respiration life was prolonged until 3 45 A M

Autopsy, six days postmortem Abstract of report Anatomic diagnosis

Chronic adhesive pleuritis

Hemopericardium

Fatty metamorphosis of the myocardium

Rupture of the heart (left ventricle)

Chronic endocarditis (aortic sclerosis)

Emphysema of the lungs

Cyst of the liver

Cholelithiasis

Chronic nephritis

Arteriosclerosis

Pleural cavities Both show a few old fibrous adhesions

Pericardial cavity Upon section, shows a layer of red clot about 5 cm in thickness, overlying the front wall of the heart, and continuous with another mass of clotted blood at the back of the cavity Weight of the entire amount of clot 300 gm In addition, the pericardial cavity contains about 100 c c of blood-stained fluid

Heart Weight 440 gm Epicardial fat moderate in amount The posterior wall at a point 3 cm below the auriculoventricular groove shows a longitudinal tear 1 cm in length, communicating through an oblique canal with the cavity of the left ventricle, and behind the posterior curtain of the mitral valve On section, the cavities are empty, myocardium pale brown, streaked with yellow, exceedingly flabby, that of the right ventricle contains, in addition, a yellowish zone bordering upon the endocardium Wall of the left ventricle 1.2, of the right 0.5 cm in thickness Mitral valve 11, aortic valve 9, pulmonary valve 10, tricuspid valve 13 cm in circumference Depth of left ventricle 12 cm The curtains of the mitral valve are somewhat fenestrated, the two anterior ones partially united by a fibrous band, within which is a calcareous nodule near their bases, cavities considerably dilated The right coronary artery originates at a point just above the junction of the right anterior and the posterior curtains, upon section, both arteries show some arteriosclerosis with calcification

Lungs Alike, voluminous, the anterior borders meet in the median line, extensively pigmented, of downy consistence throughout and of general grayish-red color, upon section, grayish red and moist, the backs dark bluish red, otherwise negative, bronchial lymph-nodes black

Liver Weight 1400 gm, shows extensive postmortem changes, the upper surface shows numerous fibrous tags and occasional blebs, the anterior border, to the right of the gall-bladder, shows a smooth-walled cyst 3 cm in diameter containing gas

Gall-bladder On section, contains multiple calculi, the

largest 1.5 cm in diameter, and black, the smallest the size of a hemp seed

Kidneys Weight of both 300 gm, upon section, capsule slightly adherent to a finely granular surface, both show extensive postmortem changes, cortex 0.6 cm in thickness

Aorta Upon section, shows considerable arteriosclerosis, with large atheromatous patches

We have, then, the history of 2 cases, one a woman of fifty-one, the other a man of eighty-one, both with advanced arteriosclerosis, and in each instance an almost helpless invalid. Case I had had a cerebral hemorrhage, with resulting hemiplegia and permanent aphasia. Death occurred almost instantly during the night, being preceded by deep cyanosis, intense distress for breath, and great suffering. Myocarditis with a tear in the right ventricle and hemopericardium were found at necropsy. The second case had a quite similar seizure, but did not die for nearly eight hours. At postmortem section the pericardium was found greatly distended, with clots and blood due to a tear in the posterior wall of the left ventricle near the apex. In neither case did the coronary arteries show any distinctive changes other than those of very moderate arteriosclerosis. No thrombosis or embolism were present.

DISCUSSION

With such a definite gross anatomic lesion it is natural that spontaneous heart rupture should have been early recognized. The first description of the condition is usually attributed to William Harvey in the latter part of the eighteenth century. Since that time it has been a subject for frequent study and report, until now one finds a rather voluminous literature on the subject. One of the most complete discussions of the condition was made by Huchard in 1899 (*Maladies de Cœur*, 1899, 1, p. 228), based on 189 cases collected by him. During the period of approximately twenty-five years since this article appeared I have been able to collect 71 typical cases from the literature, making a total, if combined with Huchard's, of 260. Although somewhat incomplete, this group is sufficiently large to afford

an opportunity for a quite accurate survey of the disease. The figures just quoted indicate that rupture of the heart is far less rare than was formerly supposed.

The general features of the condition and its course are subject to great variations, but may with reference to the duration of the former prior to death be divided into two definite groups, namely, those cases in which death is practically instantaneous, and those in which death follows the appearance of symptoms after an interval of time which varies from hours to days or even weeks. The first is somewhat more common than the second. Among the 71 cases collected, 43 died suddenly, and 16 of these were found dead, usually in bed. Case I, just described, is typical of this group. The patient, seemingly in her usual health, suddenly and without any definite cause collapses and dies. The clinical picture is quite inconstant, varying considerably in respect to the character of the individual symptoms. Actually in many cases the symptoms are almost negligible and the diagnosis is made postmortem. Usually without warning the victim is very suddenly seized with an intense pain in the lower left front of the chest, occasionally radiating to the back and left shoulder, or the pain may be confined to the epigastrium. At the onset distress over the precordia or even a "sensation of tearing" is felt. Dyspnea, often of an extreme type, quite constantly accompanies the pain and is associated with cyanosis and weakness of the pulse. Nausea and vomiting sometimes occur. The patient is pale, has an agonizing expression, and presents the picture of imminent death. Syncope and death follow. Many of the reported cases died almost instantly when the patient was walking about or sitting quietly in a chair. More frequently there is a definite interval of a few minutes between the appearance of the symptoms and the fatal termination.

The second type mentioned above presents a somewhat different picture, but chiefly in the fact that death is not immediate. It may be just as sudden and violent, however, though delayed. The onset is the same, and seemingly with just as violent symptoms, but which, after a brief period, becomes more or less relieved. Indeed, in a considerable number

of instances the symptoms have entirely cleared, apparently leaving the patient as well as ever. After an interval of hours or, more often, days the symptoms suddenly recur and a fatal issue follows. Finally, in a considerable percentage of cases the alarming condition of the patient is not in the least relieved or only slightly, and death finally results after a variable period of hours. The second case before us this morning, who lived eight hours, is typical of this group. It is important to note that in almost all of these cases where death does not follow at once, the final termination is nevertheless very sudden.

A careful study of the 71 cases collected shows some interesting facts relative to this question of the course of the disease. In 43 deaths it is mentioned as sudden. Sixteen of these, however, were found dead, usually in bed, but presumably died very suddenly. Two of these 18 cases were found dead in the lavatory. Nine lived from one to fifteen hours, while 14 lived more than one day, the duration varying from one to twenty-one days.

Reznikoff¹ reports very interesting and important observations regarding the local physical signs in a typical case. Just before death, which was of the sudden type, the author describes the auscultatory signs as follows: "A continuous muffled, low-pitched, rushing rumble, louder during expiratory phase, dimmed during the few inspiratory periods, was constantly heard." Autopsy revealed a laceration in the anterior wall of the left ventricle near the septum 3 cm. in length. Such findings must be exceptional if not indeed unique, yet some changes in the normal physical signs cannot fail to be present in at least a majority of cases if a careful examination is made. The symptoms are usually so distressing and so soon followed by death that no opportunity is afforded for any investigation of the heart. In many of the cases in which death has not occurred immediately the signs have been carefully observed and recorded. They are, in general, those of hydropericardium and failing myocardium. The area of cardiac dulness is increased, the heart sounds are feeble, with a tumultuous action. Arrhythmia is common. Signs of pulmonary congestion may appear

¹ Jour Amer Med Assoc, Chicago, 1922, lxxviii, 1296

Severe sensitiveness to pressure in the epigastrium, as in pericarditis, has been observed

Since all recorded cases of spontaneous rupture of the heart have been examined postmortem, it is evident that the records of these cases afford an unusual opportunity for a study of the pathology of the disease. First, as to the characteristics and location of the rupture. It is almost invariably linear and shows all gradations from a rough, jagged wound, with irregular edges, to a clean, straight cut, such as might be made with a sharp knife. A few striking exceptions to this common type of lesion have been recorded: a large triradiate rent on the anterior wall of the left ventricle,¹ a zigzag rupture $\frac{3}{4}$ inch long in the left ventricle,² a ragged hole in left ventricle,³ a long circular opening in anterior wall of the left ventricle,⁴ and a double opening in wall of left ventricle.⁵

When seen postmortem the tear in the heart wall is most frequently closed, although at times the edges are widely separated by clots. It is very common for the internal opening to be much smaller than the external, and, because of the nature of the inner surface of the heart chambers, very difficult to find. So completely is it sometimes concealed that it can only be located by the introduction of a probe through the outer opening into the ventricle. The size of the surface rent varies considerably, but usually is from 1 to several cm in length. In one case it is given as 5 and in another 8 cm. The course of the opening through the heart wall may be quite direct, but is more often very irregular, and in general direction oblique. Very often it has been found to follow a zigzag course.

The location of the rupture is well shown by the table on page 1678, which comprises the 189 cases of Huchard⁶ and the 70 cases collected since 1900.

¹ Davis, *Lancet*, London, 1909, 1, 1683

² Fouracre, *Brit Med Jour*, London, 1909, 1, 276, Sturrock, *Brit Med Jour*, 1906, 1, 500

³ MacCallum, *John Hopkins Hosp Bull*, Baltimore, 1908, vii, 50

⁴ Rebattu and Jossierand, *Lyon Med*, 1923, cxxxii, 411

⁵ Tapie, *Progrès Méd*, Paris, 1917, xxxii, 314

⁶ *Maladie de Cœur*, 1899, vol 1, 229

	Number	Per cent
Left ventricle	207	79.9
Right ventricle	26	10.1
Both ventricles	6	2.3
Left auricle	7	2.7
Right auricle	12	4.6
Interventricular septum	1	.4
Total	259	100.0

You will see from this table that in approximately 80 per cent of cases the rent is in the left ventricle, and, roughly, 93 per cent in one or the other of the ventricles. Furthermore, in nearly all cases the favorite site of the tear in the ventricle is the anterior wall near the middle or toward the apex, although almost never at the actual tip of the ventricle. The reason for this preference for a particular portion of the left ventricle will be discussed a little later. Among the 57 cases of left ventricle rupture in our total of 70, only 5 were of the posterior wall, the remainder all being anterior.

The condition of the pericardium in the reported cases is almost uniformly of a given type. The sac is greatly distended, deeply cyanotic, and of a dull luster. Fluctuation is a striking and constant feature. When incised the distention is found to be due to the pressure of fluid blood and clots, the latter often adherent to the visceral pericardium. The usual amount of blood is a few hundred cm., but in Sturrock's case¹ was 29 ounces. As a rule no marked changes are seen in the pericardium, though occasionally in cases where death does not follow immediately pericarditis may develop.

It has long been an accepted principle that heart rupture of the type which we are discussing today never occurs in the normal heart. In other words, spontaneous rupture of the heart occurs only in individuals with very severe disease of the heart muscle (v. Jurgensen's law). The reports of cases for the past twenty years give quite definite and fairly uniform accounts of both gross and microscopic abnormalities in the heart muscle. The myocardium in the immediate vicinity of the tear is never normal. Necrosis with hemorrhagic infiltration of the muscle is often seen for a considerable area surrounding the

¹ Brit. Med. Jour., London, 1905, i, 503

rupture The condition suggests that the blood is forced into the diseased muscle in the same manner as in the dissecting aneurysm The most common change described is a so-called fatty degeneration, which is frequently combined with a "local softening and thinning of the muscle" Changes in the heart-muscle in such areas are in the end particularly prone to take the form of a diffuse fibrosis, which, in turn, may lead to an aneurysm of the heart wall

The most common cause of these changes is generally believed to be coronary sclerosis, with occlusion of some branch, and a resulting infarct In the vast majority of cases it is the descending branch of the left coronary which is occluded, a fact which explains the predominance of the anterior lower wall of the left ventricle as the site of rupture In 25 of our 70 collected cases an actual blocking of some branch of the coronary artery, with resulting infarct, was recorded But there are many typical cases in which neither occlusion of the vessels nor infarction have been found, and it is clearly impossible to explain all cases on this single basis Extensive local muscle alterations, usually designated as "fatty degeneration," and without significant coronary changes, are described in a considerable number of instances It is perfectly possible that these changes may be the result of thrombosis of some small branch of the coronary, with resulting infarct, which is overlooked

A less common condition tending to rupture is the infectious myocarditis with embolic abscesses of the heart wall which occurs secondary to various infectious diseases and septic conditions (smallpox, scarlet fever, typhoid fever, erysipelas, septicopyemia) Ulcerative endocarditis can also invade the heart muscle in the same manner Syphilis plays a not insignificant rôle 9, or 12.8 per cent, of the 70 cases had syphilitic lesions of the myocardium to which the rupture could be definitely attributed Among these 9 cases, 4 showed coronary obliteration due to lues, and 3 gummata of the heart wall with rupture Congenital syphilis and sepsis are the cause of spontaneous heart rupture in the vast majority of cases appearing before middle life

Tumors, cysts, and tuberculosis comprise a small group which may rarely cause changes in the heart muscle sufficient to lead to rupture. One case is reported in which rupture followed the passing of a stomach-tube. This accident to the heart occurs so commonly in the insane as to seem significant. 10 of our 70 cases were insane, while 2 others were epileptics.

Briefly, then, one sees from the foregoing that a considerable variety of causes may produce heart rupture through weakening of the muscle wall. The usual sequence of events, however, is the obliteration of a coronary vessel, with the formation of an infarct resulting in degenerative changes in the heart muscle, and finally rupture. Many have contended with Parrot that "fatty degeneration of the muscle is of all the causes of rupture the most common," but the studies of recent years tend definitely to show that the most common cause of the degeneration found is coronary obstruction from embolism or thrombosis with infarct formation. It seems probable that many of the cases recorded as due to fatty degeneration are actually instances of muscle degeneration following infarction from coronary occlusion, which was not found.

In a rather surprising number of cases there is unmistakable evidence that in addition to the main factors discussed above other immediate or secondary causes play a part. Such causes are those which, as a result of a severe physical exertion, bring a sudden and severe strain on the heart. From among the many such causes the most commonly mentioned are heavy manual labor, epileptic attacks, prolonged vomiting, and coitus. Great excitement of any kind or intense emotional disturbances should also be included in this group.

Certain other etiologic considerations are of more or less interest and importance. Figures for 276 cases collected by different writers on the subject show that 199, or 72 per cent, were over sixty years of age, and bear out the accepted fact that the disease is one primarily of old age.

Males are somewhat more frequently affected than females, the ratio being about 7 : 5.

Considerable stress has been laid on the general hygiene of

the patient as having an important etiologic relation to the condition, but it is difficult to imagine anything other than a very remote and indirect one

The mechanism of spontaneous rupture of the heart is not altogether clear, but regarding many of its features there is a general agreement. The pathologic processes just discussed are not general throughout the heart, but confined to one or occasionally more quite definite areas. Thus, a given small portion of the heart wall becomes weak through degenerative changes, while the heart as a whole remains strong and capable of maintaining a high pressure. Under this pressure it is inevitable that sooner or later the heart wall at the point where its resistance is greatly diminished by reason of necrosis and fatty and fibrous degeneration should give way. If the tear in the muscle is complete, death follows almost instantaneously. The onset of symptoms probably coincides with the actual rupture of the heart wall, though in the cases of slow evolution it may mark the formation of the infarct. Considerable controversy centers about the question of the cause of death in either the traumatic or spontaneous form of heart rupture. It is generally believed that death results directly from the sudden increase of pressure within the pericardium, which, when it reaches a certain height, makes further contraction of the heart impossible. Hopkins¹ believes that as pressure of the blood in pericardium approaches the equal of that in the right auricle it interferes with the entry of blood into the heart from the great veins. This same author quotes Cohnheim's experiments on dogs as showing that the sudden injection of 150 to 200 c c of fluid into the pericardial sac is sufficient to cause death, also that a much larger amount can be introduced without fatal results if injected slowly. In some cases it is impossible to explain the sudden death on this hypothesis. Many authors consider that death is due to reflex causes even in cases of severe hemopericardium. Ramond and Baudouin² are strong advocates of this theory. They cite as proof of this hypothesis that

¹ Proc. New York Path Soc., 1910-1911, n s., v, 200

² Medecine, Paris, 1921, 1922, II, 426

in some of the most rapidly fatal cases no blood appears in the pericardium, and in many cases of infarction of the heart wall sudden death occurs without rupture or hemorrhage

Considerable controversy likewise has centered about the question as to the period of the heart cycle when rupture takes place. Many of the older writers believe that the heart wall gives way only during diastole, but, on the other hand, as argued by Huchard, the intracardiac pressure is greatest during systole, therefore this is the time most dangerous to a weakened heart muscle

Diagnosis of spontaneous rupture of the heart has seldom been made except at the autopsy table. Since the condition presents no pathognomonic symptoms or signs, a positive ante-mortem diagnosis is practically never certain. If, however, the possibility of such an accident be kept in mind, and especially under certain conditions, then we may occasionally, at least, be reasonably sure of its presence. One should think of the possibility of cardiac rupture in every individual over sixty in whom a sudden severe precordial or epigastric pain of anginal type suddenly develops and is quickly followed by syncope and death. In these cases there is, by reason of the immediate fatal termination, no opportunity for x-ray and other special methods of study, or, as a rule, even a careful examination of the heart to aid in diagnosis. To differentiate the condition from a fatal attack of angina pectoris is impossible, as the pain is a true cardiac angina.

The agonizing pain, if in the epigastrium, always suggests an acute abdominal condition, but the latter can be ruled out because of the immediate death. Apoplexy, likewise, which is so often wrongly spoken of as a common cause of very sudden death, can be excluded, since in cerebral hemorrhage unconsciousness may be sudden, but death almost never results under twenty-four hours. There is, in fact, no real resemblance in the two conditions.

It is in the second group of cases, namely, those of slower evolution, that a better chance of correct diagnosis is offered. The picture as given earlier in the clinic is quite distinctive of

rupture, though it seems to me identical with that of coronary thrombosis. As suggested also, the symptoms at onset in this slowly developing form of rupture probably are actually due to the formation of an infarct from embolism or thrombosis in the coronaries. The partial or complete relief of symptoms for an indefinite period of hours to weeks, to be followed by the sudden or gradual development of dramatic symptoms of agonizing pains, striking general appearance of collapse, and finally syncope and death, are very characteristic of a ruptured heart muscle. Physical signs when a cardiac examination can be made sometimes give material assistance. The signs are those of fluid in the pericardium and cardiac failure.

But little need be said regarding prognosis. It is evident from the discussion of the condition and its course that death is inevitable, yet cases are recorded which showed healed rupture of the heart at postmortem examination.

1

CONTRIBUTION BY DR JOSEPH H PRATT

BOSTON

GOUT

Incidence in America —Whether gout is a rare or a common disease in this country is a mooted question Sir Dyce Duckworth¹ wrote in 1890 that gout was "practically unknown in America" Sir William Osler² thought it was common in the United States, and so states in the latest edition of his text-book The records of the Johns Hopkins Hospital certainly supports this view There were 92 cases among 30,871 medical admissions to that hospital (Fletcher³) Dr Osler did not always regard gout as common in America, for in a paper⁴ published in 1895 he stated that "the comparative infrequency of gout is a matter of every-day comment" It was the experience at the Johns Hopkins Hospital apparently that led him later to change his opinion These statistics compared with those of St Bartholomew's Hospital, London, indicate that gout is only one-third less frequent among hospital patients in Baltimore than in London In Chicago among the poor people who seek treatment in the public wards of a hospital gout is apparently even more frequent than in Baltimore Williamson⁵ in 1920 reported a series of 116 cases of gout admitted to the Cook County Hospital during a period of six years Tophi in the ears were present in 65 of these patients I have been told by Chicago physicians, however, that among the well-to-do in that city gout is rarely seen Inquiry of physicians living in different parts of the United States and Canada has failed to reveal any locality in which the disease is commonly seen in private practice It is certainly true that a larger series of cases than that of Williamson has never been reported in America, and those, it will be

noted, were drawn entirely from hospital practice. Although the incidence of the disease is said to be decreasing in England, Lindsay,⁶ of Bath, reported in 1913 a series of 569 cases of gout seen in his private practice.

Far larger series of cases have been reported from Germany than from our country. Umber,⁷ for example, stated that he had studied in his consultation and hospital practice 278 cases up to 1914. While practising in Hamburg Altoona, among the 2300 cases he saw in consultation practice, 110 were gout. This equals 4.7 per cent of all cases seen. Minkowski⁸ had 48 cases of gout, or 2.8 per cent, in a series of 1700 cases seen in consultation while he lived in Cologne.

The disease has always been regarded as a rare one in New England. The only one to express a different opinion, so far as I know, was W. H. Draper,⁹ who wrote forty years ago in *Peper's System* that while acute articular gout was said to be uncommon in New England irregular forms of the disease were frequently seen here. Their occurrence he attributed to cider, which was always a popular alcoholic beverage in this section. As we now know the so-called irregular forms of the disease of older writers were not gout, Draper's statement can be dismissed from consideration. If gout occurred in Boston a generation or more ago it was rarely recognized, at least in hospital practice. From the opening of the Massachusetts General Hospital in 1821 until 1910 there were only 29 cases in the wards diagnosed as gout. From 1910 until 1923 no less than 32 cases were recognized as gout. These figures show that more cases of gout have been seen at the Massachusetts General Hospital in thirteen years beginning in 1910 than in the previous eighty-nine years! They suggest that gout is now more often recognized at this hospital, rather than that the frequency of the disease is rapidly increasing. The first case diagnosed as gout was admitted in 1845, twenty-four years after the opening of the hospital. I have looked up the clinical records of this case. The characteristic features of the disease, if they were present, were not brought out in the notes. There was no mention of tophi. The inadequate description of this first case raises the suspicion

that little was known by the attending physicians at that time about gout and its diagnosis. Although gout may have been rare in Boston in the middle of the last century, it did exist here, for in the Warren Museum of the Harvard Medical School may be seen today some interesting specimens that date from that period. The earliest specimen is a big toe-joint with a deposit of urates. It was acquired in 1852. The catalogue¹⁰ states that it was removed from the body of "a man aged fifty-two of intemperate and dissolute habits," who died at the Massachusetts General Hospital of Bright's disease. Over one of the joints immediately beneath the skin was "a white pasty substance," which Dr. John Bacon found to consist of "urate of soda with a little chlorid of sodium and phosphate of lime and a considerable proportion of animal matter." In 1854 Dr. R. M. Hodges gave the museum a collection of over 60 bones from a dissecting-room subject. Each bone is marked by incrustations of sodium urate on its articular surface. The hip-joint is very rarely attacked in gout, but in the remarkable case shown here it is seen lined with a deposit of urates. There is an excellent plaster cast of the deformed hand of a patient with severe chronic gout who was in the hospital in 1863. He had the disease for years, the catalogue¹⁰ records, "and in some places the white deposit could be seen through the cutis." These specimens are well worth a visit to the museum to anyone interested in the pathologic anatomy of gout.

The discovery by Professor Folin in 1912 of a method of determining the quantity of uric acid in the blood attracted world-wide attention and naturally led to a more careful search for cases of gout in the local hospitals. The uric acid in normal blood Folin found by his original method to range from 1 to 2 mg per 100 c c. I remember well the first case of gout in which the blood was examined, and the suppressed excitement I felt before the result was known. The subject was a private patient of mine, and Dr. Folin journeyed with me to the Corey Hill Hospital and obtained the blood himself. The analysis showed 5.5 mg of uric acid per 100 c c of blood, which was about twice the normal amount. In a paper with Dr. Denis¹¹ he published the

analysis of the blood in this and 5 additional cases of gout, but in none of the others was as much uric acid found as in this first case

As relatively few gout cases require bed treatment except in acute attacks, it might be expected that the out-patient records of the Massachusetts General Hospital would show a greater frequency of gout than the in-patient statistics indicated. This is found to be true. The number seen among the ambulatory patients, however, was not large. From August, 1903 to May 15, 1916 among 298,000 patients admitted to all the clinics, the diagnosis of gout was made 42 times.

Some critics claim that gout is frequently overlooked even at the present time. It would be interesting to know how many cases are seen in a hospital in which special attention has been paid to the study of the disease. Such an institution is the Peter Bent Brigham Hospital. It was not opened until after Dr. Folin's methods for determining uric acid in the blood were available for the study of gout, and they have been much used there as an aid in diagnosis. Dr. Christian has always been keenly interested in gout, and, what has been of equal importance, he has justly insisted on the uncertainty of the diagnosis of gout in chronic arthritis unless tophi could be found. Soon after the opening of the hospital Dr. McClure and I began, through the courtesy of Dr. Christian, a study of the uric acid in the blood and urine in a series of cases. Later McClure made studies of the kidney function in gout, and, with McCarthy, an important investigation of the changes in the bones as revealed by the Roentgen ray. Dr. Christian has published a clinical report in which he emphasized the similarity of the x-ray pictures in gout and non-gouty arthritis. More recently Folin, Berglund, and Derick have made valuable studies on cases of gout that were under observation or treatment in Dr. Christian's wards. These various investigations carried on during the past ten years must have tended to make the entire medical staff more alert in the recognition of gout than they otherwise would have been.

I have analyzed all the cases of gout that have been admitted

to the Peter Bent Bringham Hospital from its opening in 1913 to November, 1924. There were 44 cases among the 24,766 admissions to the medical wards. A few of the cases were admitted more than once. As a result the number of admissions in which the diagnosis of gout was made totaled 55, although, as stated, there were only 44 cases. The percentage of gout to the total medical admissions was 0.22. This is lower than at the Johns Hopkins Hospital, where the percentage was 0.29. The incidence of gout in the wards of Cook County Hospital, Chicago, according to the published statistics is 0.39 per cent. This is a little higher than in St. Bartholomew's Hospital, London, the home of gout, where the percentage was 0.37. The Bringham percentage is high compared to the extraordinary low figure at the Massachusetts General Hospital during the period between 1821-1916, where the percentage of gout to total medical admissions was only 0.03¹.

All published statistics of gout should be examined very carefully before they are accepted, as the diagnosis is often made on insufficient evidence. Unless tophi are found the diagnosis of a gouty diathesis lacks complete proof. No one doubts that gout without demonstrable tophi is fairly frequent, but the more carefully cases are investigated, the larger is the percentage in which tophi are found. In drawing conclusions regarding the incidence of the disease from any collected series of gout cases one should determine on what criteria the diagnosis was based, and especially in what percentage of cases tophi were present. The high percentage of cases found at Cook County Hospital might arouse suspicion that other arthritic conditions had been mistaken for gout, were not the fact stated that tophi were found in the ears of 65 of the patients. That forms a goodly percentage of the total number of 116 cases of gout, namely, 56 per cent. Futcher,¹² in a paper on gout, reported that tophi were found in 17, or 47 per cent, of the first 36 cases studied at the Johns Hopkins Hospital. In 15 of these cases tophi were present in the ears. In the Bringham series tophi were found in 26 of the 44 cases, or 59 per cent. It is thus seen that in these three series the percentage of cases in which tophi were found did not

vary greatly, as it ranged from 47 to 59 per cent. In the English series studied by Lambert tophi were present in 52 per cent. This figure agrees well with the American findings. It was highest, it will be noted, in the Brigham cases. In examining the analysis made of some series of cases this valuable guide to the accuracy of the diagnosis, namely, the percentage of cases with tophi, is absent. This is true, for example, in the largest series ever reported, that of Lindsay, which consists of 569 cases. The critical student before attaching importance to his conclusions would like to have doubts regarding the accuracy of the diagnosis removed.

Gout in Women.—Since the time of Hippocrates¹³ gout in women has been rare except during the period of the Roman Empire, when women vied with men in gluttony and other vices. Among 92 cases of gout at the Johns Hopkins Hospital there were only 4 women. In Williamson's Chicago series there was only 1 patient of the female sex in the 116 cases, an incidence of less than 1 per cent. At the Brigham Hospital 4 of the 44 cases were in women. In none of the 4 were tophi present, and I am doubtful if 2 of them were really gout. Not only are tophi rare in females, but involvement of the big toe is less common than in males. It is often impossible to make a definite diagnosis of gout in women. I have studied 2 cases with definite podagra in women in whose blood the uric acid was not increased, and hence it is doubtful whether the inflammation of the big toe was due to gout. The greater the number of cases of gout among women in any series, the more suspicious we should be of the value of the statistics. In a study by a commission of the French Academy there were only 2 women among 80 patients with gout. The disease is relatively more common among women in England than in America. Lambert,¹⁴ of Cambridge, England, reported 23 cases in women in a series of 125. The percentage of female patients, 18.4, is unusually high, so high, in fact, that doubt of its correctness is warranted in spite of the occurrence of tophi in 9 out of the 23 women, that is, 39.1 per cent. In Lindsay's study of 569 cases observed at Bath, England, he included 87 among women. That makes a percentage

of 15 3, which, although less than Lambert's is still suspiciously high. One's skepticism of the correctness of his diagnoses is confirmed by his statement that "women suffer from gout in a slow smoldering sort of way, which never actually bursts into flame. It is among women that we have the most typical example of the suppressed, incomplete, or asthenic forms of gout. They frequently complain of little more than 'chronic rheumatic pains' in the fingers and other joints. The hands become enlarged and gnarled and show Heberden's nodes"¹⁵

There is not a scintilla of evidence that women with these vague indefinite symptoms have gout, while there is much evidence that they have not that disease. If they have the gouty diathesis they would be expected to have hyperuricemia, yet the blood of the cases of this type has not shown any increase of uric acid. Lindsay's statement indicates that he regards Heberden's nodes as a sign of gout. This is a common error that has often misled the unwary. Yet the wisest clinical observers from the time of Heberden, as well as Heberden¹⁶ himself, have agreed that the nodes are in no way related to gout.

My doubt of the accuracy of the diagnosis in Lindsay's cases in women is supported by the statement of a leading English authority, Llewellyn, whose observations have been made at the same place as Lindsay, namely, Bath. Llewellyn¹⁷ writes as follows: "From my own experience, the figures submitted to the French Academy (2 women to 78 men, J. H. P.) probably represent the ratio of incidence in males as opposed to females. This certainly, if regular, in opposition to 'irregular' types of gout be the criterion, for it must be admitted that regular gout does occur in women, though exceptionally rare either prior or subsequent to the climacterium.

"As to the current opinion that the regular manifestations of gout in women are of asthenic, as opposed to sthenic character, this has, I think, often proved a source of fallacy. At any rate, in many cases the assumed gouty inflammation resolves itself into one of inflamed bunion. Again, in but too many instances, women showing Heberden's nodes are held to have gout or 'rheumatic gout.' The latter term, as Pye-Smith observed,

'is a bad name for osteo-arthritis,' to which category Heberden's nodes belong

"Judged by the one unequivocal criterion—*e*, tophi—gout in women is extremely rare. If to this be added the further fact, viz, the rarity in their sex of classical attacks in the great toe, we see clearly that the diagnosis of gout in women is often a matter of assumption rather than of certitude." My own experience convinces me of the truth of Llewellyn's conclusions. In America Heberden's nodes and other forms of osteo-arthritis are as common in women as gout is rare.

The Occurrence of Tophi—As tophi form the only pathognomonic sign of the gouty diathesis, a careful search for them is of the greatest importance in the diagnosis of gout. The word "tophus" is derived from the Hebrew and means concretion. These deposits were formerly called chalk-stones, from the mistaken idea that they were composed of chalk or calcium carbonate.

Tophi are most commonly found in the ears. Garrod,¹⁸ who first discovered this fact, noted their presence in 17 cases out of 37 examined. They occurred in the ears alone in 7 cases, in the ears and around the joints in 9, and in 1 case only were they recognized in other parts of the body without being present in the ears also. Dr Osler impressed forcibly upon his students the importance of carefully examining the ears for tophi in the routine examination of patients. Dr Christian, following the teaching of his master, has insisted that on the clinical note of the physical examination of all patients admitted to the medical wards of the Brigham Hospital the presence or absence of tophi in the ears should be noted.

In the Brigham series of 44 cases tophi in the ears were found in 22 of the patients. In 4 others there were tophi on the hands, but not in the ears. There was a total of 26 cases with tophi in the series of 44 cases of gout, or a percentage of 59. It is interesting to compare this result with that of others. Garrod¹⁸ found tophi in 46 per cent. Fitcher,¹² in his first analysis of a small series of 36 cases observed in Osler's wards, stated that tophi were present in 17, or 47 per cent. They were located in

one or both ears in 15 cases, in the "subcutaneous tissues over the elbow-joint" in 4, and in 1 over the patella In the Cook County Hospital cases tophi were demonstrated in 66 of the 116 patients, or 57 per cent Tophi were found in the ears of 65 patients In only 1 were they present elsewhere when not in the ear In 14 patients the tophi were present elsewhere as well as in the ears The various situations were the fingers, toes, elbows, and thyroid cartilage In the various series here compared the highest percentage of cases with tophi was the one I am now reporting from the Brigham Hospital

The predilection of tophi for the ears is remarkable, as is shown by the fingers here presented Out of a total of 126 cases with tophi in 118, or 94 per cent, the urate deposits were found in the ears

Careful examination of the ears is necessary, as the presence of tophi when of small size is easily overlooked The tophi are usually situated on the margin of the ear, but may be on the antihelix or the pinna They are formed beneath the skin and are sometimes quite firmly attached to the cartilage In size they vary from a pinpoint (Garrod) to a pea They are frequently not larger than the head of a pin The skin over a newly formed tophus may be natural in color, and the deposit then may be more readily felt than seen More frequently, according to Llewellyn's experience, the skin is red over a forming tophus Usually the tophi when first seen have existed some time and the skin is yellow or white and opaque Small sebaceous cysts, milia, and tiny projections of the cartilage of the ear may be mistaken for tophi The diagnosis of a tophus should not be made without removing some of the contents of the nodule and demonstrating with the microscope the presence of the typical needle-shaped crystals of sodium urate The contents are usually easily removed with a needle without pain On opening a fresh tophus a milky fluid exudes Later the fluid is changed to a chalky consistence

The necessity of careful examination of the ear is shown by the records at the Brigham Hospital In 2 or 3 of the cases the positive statement was made by the house officer in the note on

admission that no tophi were in the ears, while at another examination made by one of the senior members of the staff a few days later tophi were discovered. Patients sometimes remove the nodules themselves and may even note the peculiar chalk-like appearance of their contents. Hence it is important to inquire carefully, if gout is suspected, whether nodules have been present at any time on the ear or elsewhere, and if whitish material was obtained from them. It is well known that tophi may come and go. The idea commonly held that tophi do not form until several years after the first attack of articular gout is untrue. Their appearance may accompany or even precede the first seizure. They have been present in large numbers beneath the skin of patients who have never had any arthritis, as Trousseau¹⁹ pointed out many years ago.

The following case observed in my own practice illustrates the truth of the above statements. It shows (1) that tophi may be present and yet unnoticed owing to lack of careful inspection, (2) that even very small nodules should be subjected to microscopic examination, (3) tophi may form at the time of the first attack. Furthermore, it is an example of a mild form of the disease, possibly more common in America than Europe, in which the initial fit of gout may last less than twenty-four hours.

Frank S., aged fifty six, consulted me on May 12, 1921. He complained of slight headaches, slow pulse, high blood-pressure, and "rheumatic" pains. A definite history of two attacks of acute gout was obtained. The first seizure was in the winter of 1918-19. He awoke one night about 11 P. M. with severe pain in the right metatarsophalangeal joint. The pain kept him awake the greater part of the night. The next morning the joint was red and swollen. He rode to the factory where he worked. The pain disappeared during the day, and he slept well the following night. He was able to wear an ordinary shoe the next day. The foot did not pain him. In fact, there was no return of pain until his second attack a year later. This also began in the middle of the night, and involved the big toe. He got out of bed to apply liniment to the foot. After resting about

half an hour on a couch he attempted to return to bed, but when he put his foot on the floor the pain was so intense that he could not take a step. The pain when at rest was so severe that he got no sleep at all that night. The pain continued throughout the following day without remission. The morning of the second day the knee and the big toe-joint were much swollen and the latter as "red as beef." If anyone touched it he "yelled." He was two nights and two days on the couch, and did not get back to bed until crutches were procured on the third day. The pain ceased quite suddenly, as after the third day he had no pain in the foot except on walking. He had never taken much alcohol. He formerly ate meat three times a day, but never a large amount. There was no family history of gout.

I examined his ears for tophi at the time he first consulted me, but found none. At his second visit two days later he volunteered the statement that the previous summer (1920) he had removed a nodule containing "chalky material" from his right ear. It was then the size of a pea. He had first noticed it at least two years before he removed it. (If so, the tophus developed in or before the summer of 1918, fully six months prior to his first attack of podagra.) It grew steadily in size.

At the time of this visit I wrote the following note: "The other day on looking at the ears I did not see any tophi. Today, on careful examination, I discovered a tiny yellow nodule, about the size of a pinhead, on the outer rim of the ear. On opening it a small amount of chalky material was expressed. Under the microscope this consisted of a small mass of epithelial cells and, in addition, there was a group of acicular crystals of sodium urate. The needle-shaped crystals were unusually long. Near the lower border of the same ear was another small nodule, similar in size and appearance to the one removed, but less yellow in color. The patient says he has frequently in the past expressed blood from it. I could not remove it with a needle and it bled freely. Examination under the microscope of the bloody fluid obtained from it showed only erythrocytes and epithelial cells."

This case brings out strikingly not only the need of most careful inspection of the ears, but of removing the contents of any nodule that may be present. The demonstration of the typical crystals of sodium urate is necessary before the evidence that a tophus is present is complete. Small sebaceous cysts and small elevations of the cartilage itself may easily be mistaken for tophi.

When tophi occur elsewhere than on the ears the examination is not complete until some of the contents have been removed and the typical crystals found with the microscope. Material can readily be removed from soft tophi by plunging a hollow needle into them and aspirating some of the contents with a small syringe.

Among physicians in Massachusetts and doubtless elsewhere there is wide-spread ignorance of the significance of the chalk-like contents of tophi. The experience of the patient, Willard G., testifies to the correctness of this statement. When I saw him in 1916 his hands were greatly deformed by tophi. There were 13 sinuses discharging chalky material on his left hand and 7 on his right hand. When he consulted me the diagnosis of gout had been made that day for the first time, although he said 8 doctors during a period of six years had seen the white opaque material exuding from the ulcers on his fingers. The diagnosis was made by Dr James B Ayer. The patient was referred to him by a physician of large experience who thought the lesions on the hands were syphilitic. Dr Ayer transferred the patient to me, and the history I obtained contained the following points of interest. He was a negro forty-three years of age. The first attack, which involved the big toe, tarsus, and ankle, occurred at the age of twenty-five. He had a great many subsequent attacks. The inflammation was confined to the feet for five or six years, then the elbow became inflamed. "About six years ago the left thumb began to swell and was so painful that he could not sleep. One night, the pain being intense, he thrust a needle into the swelling, and white material, 'looking like putty,' exuded. This soon hardened and then resembled 'plaster of Paris and was just as white.' After the

swelling was opened the pain disappeared. An ulcer still remains six years later. During the eighteen years he had suffered from gout he had consulted, he said, about 14 doctors, and none of them made a diagnosis of gout."

Large tophi on the feet or hands produce great deformity. The shape of the fingers may be so distorted in extreme cases that they may resemble a bunch of parsnips as Sydenham said,²⁰



Fig 251 —Large tophi on the feet. The tophus on the little toe was removed (see Fig 252) (Courtesy of Dr Frank Billings)

more than a part of the human hand. A large tophus above the metatarsophalangeal joint of the big toe of the right foot is shown in Fig 251. On the little toe of the left foot is another tophus of considerable size. The photograph was given to me by Dr Frank Billings of Chicago, and has never before been published. The patient was in the Presbyterian Hospital in the service of Dr A D Bevan, and Dr Billings was called to see him in consultation. At that time the patient was fifty-

seven years old. He had suffered from gouty attacks for a period of eighteen years. The swellings on the toes were first noticed about five years before his admission to the hospital. The tophus on the little toe as it appeared after it was removed is well shown in the second photograph (Fig 252). Note the whitish material which forms the base of the ulcer. This is the chalky substance of the older writers. It is not chalk, of course, but sodium urate. On cross-section the mass is seen to be made up of this white opaque material. As the shape of the

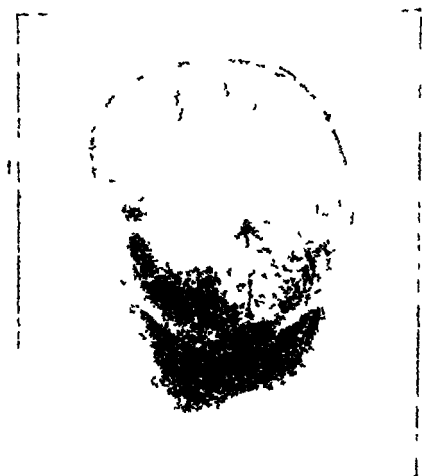


Fig 252—Tophus removed from little toe shown in Fig 251. Note the whitish material (sodium urate) in the base of the crater-like ulcer (Courtesy of Dr Frank Billings)

nodule has not been altered by sectioning it, the tophus must have been hard and firm (Fig 253)

The enlargement of the base of the big toe by tophaceous deposits may be great and the deformity produced in severe gout fairly typical. Figure 254 is from the photograph of a patient I saw with Dr Mark J Rogers, in the orthopedic ward of the Massachusetts General Hospital. The skin over the metatarsophalangeal joint of the right foot was thinned, and the white spots are due to sodium urate deposits directly beneath the skin.

All parts of the body should be examined for tophi, although the usual sites have been mentioned. Unusual locations are the edge of the eyelid, the thyroid cartilage, the vocal cords, and the corpus cavernosum.

Olecranon Bursitis—The frequency with which the olecranon bursa becomes inflamed in gout is not generally recognized. A swelling over the tip of the elbow is produced by the distention of this bursa. This condition was known to Sydenham,²⁰ who says "Sometimes the morbid matter fixes on the



Fig. 253—Cross-section of the same tophus (Fig. 252). It is seen to be composed of masses of sodium urate separated by strands of connective tissue. (Courtesy of Dr. Frank Billings.)

elbows and raises a whitish tumor almost as large as an egg, which gradually grows red and inflamed.' The bursal sac is directly below the skin, and when filled with tophaceous material may be mistaken for an ordinary subcutaneous tophus by one unfamiliar with the fact that the olecranon bursa is a frequent site for the deposit of sodium urate. Acute olecranon bursitis is a condition with which the older English writers were familiar, but in our day one rarely has the opportunity to see a case during the height of the inflammation. Scudamore²¹ says that this bursa may become distended with fluid in the course of a single

night There may be great pain and marked swelling and redness of the surrounding parts One day at the hospital I saw one of my gouty patients lying on an operating table in the surgical out-patient department The olecranon bursa was dis-



Fig 254—Tophaceous deposits about the metatarsophalangeal joint of the big toe This type of deformity of the foot is not uncommon in severe chronic gout

tended The skin not only over the bursa but over the entire upper portion of the lower arm was tense and red and the subcutaneous tissues swollen The picture presented was that seen in a severe spreading streptococcus phlegmon The tentative diagnosis was a deep abscess near the elbow An attempt

was to be made to find pus by making free incisions. With some reluctance the surgeon yielded to my persuasion to give cinchophen as he was skeptical that a gouty inflammation could produce such a clinical picture as this acutely inflamed elbow and forearm presented. The patient took the cinchophen and the pain and inflammation rapidly subsided.



Fig 255 —Distention of both olecranon bursæ in gout (Courtesy of Dr Frank Billings.)

Chronic olecranon bursitis was noted in 4 of the 44 cases of gout in the Brigham series or nearly 10 per cent. Among Williamson's 116 Cook County Hospital cases it was observed only 3 times. The much rarer condition, acromion bursitis, occurred once. In Fletcher's original report of 36 gout cases studied at the Johns Hopkins Hospital he stated that in 4 cases

tophi were found in the "subcutaneous tissues over the elbow-joint" As he did not mention the occurrence of olecranon bursitis it seems fair to assume that some if not all of these 4 were examples of the condition In Dr Billings' case already mentioned there was double chronic olecranon bursitis The characteristic appearance of the elbow when the bursa is swollen is shown in the photograph of this patient (Fig 255).

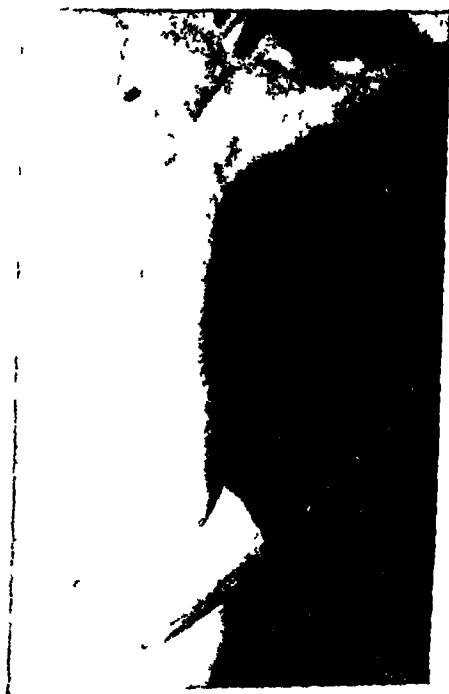


Fig 256 —Characteristic contour of the elbow in chronic olecranon bursitis

The contour of the elbow in chronic olecranon bursitis of gouty origin is also shown in Fig 256 This is a photograph of one of my patients The hands and feet were deformed by tophaceous deposits

The importance of gout in the etiology of olecranon bursitis, as well as the importance of olecranon bursitis in the diagnosis of gout, have not been generally recognized For example,

R B Osgood,²² the American orthopedic surgeon, in his recent monograph (1924) on the Surgical Lesions of Bursæ, does not mention gout in his discussion of the etiology of olecranon bursitis, nor does Telford,²³ the Englishman, who wrote the article on Bursitis in Choyce's System of Surgery (1923). On the other hand, the Germans, Wilms and Guleke,²⁴ state in the Handbuch der praktischen Chirurgie (1922) that "tuberculosis and gout play an important rôle in the etiology of chronic bursitis olecrani." The chronic inflammation of the olecranon bursa is called miner's elbow by American Surgeons, who attribute it to traumatism. It would be interesting to determine the amount of uric acid in the blood of some of these patients and to search for other evidences of gout. Brugsch²⁵ examined the blood of about 40 cases of olecranon bursitis and found the uric acid increased in all of them. When fluid or solid material are not present in the sac of the bursa the existence of a chronic bursitis can be recognized by a thickening of the walls of the sac. Brugsch goes so far as to maintain that the smallest collection of fluid in the bursa or the thickening of its wall is diagnostic of gout.

Summary—The evidence seems conclusive that gout is rare among those who seek hospital treatment in Boston. The disease is frequently unrecognized by physicians even when it presents itself in its most typical form. Among the well-to-do it is probably much rarer in America than in Europe. Gout is very rare among women. There is no evidence that the so-called irregular forms of the disease have anything to do with gout. Published statistics regarding the incidence of gout should be examined critically. The larger the percentage of cases reported in women, the greater the doubt that the data presented are trustworthy. The occurrence of tophi, when the clinical diagnosis is confirmed by the microscopic demonstration of sodium urate crystals, is proof of the existence of gout. The larger the percentage of cases reported with tophi, the greater the evidence that the data presented are trustworthy. Swelling of the olecranon bursa is common in chronic gout. It was found in nearly 10 per cent of the cases in the series here reported from the Peter Bent Brigham Hospital.

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CLINIC OF DR ROGER I LEE
NEW ENGLAND DEACONESS HOSPITAL

VASOMOTOR RHINITIS AND HYPOTHYROIDISM

ONE of the most obstinate and most exasperating conditions that concerns the internist is the patient who has repeated or continuous "colds." Such a patient is ordinarily referred to a nose and throat specialist. In a certain percentage of cases some chronic source of infection in the tonsils or sinuses, etc., will be found, and the removal of this source of infection will be accompanied by marked alleviation of the symptoms. Only too often, however, local procedures upon the upper air-passages are not accompanied by any improvement. Ordinarily the next step is a careful x-ray of the chest. Depending upon the conservatism of the roentgenologist the x-ray interpretation is variable and usually reassuring, but sometimes alarming. In children an increase in susceptibility to colds seems at times definitely associated with hilum tuberculosis, which can be diagnosed by relative malnutrition, a positive x-ray, and a positive tuberculin test. In case the x-ray picture of the chest is essentially negative, the next logical step is determination of possible sensitiveness to proteins. This may well include testing against antigens prepared from the patient's excretions. In case all of these procedures are essentially negative, one is thrown back on that glittering generality of "a run-down condition." For such patients rest, general hygiene, change of climate, etc., are usually prescribed. Within this category seems to be a group of patients, presumably small, in whom there is a definite constitutional derangement, and in whom the application of the appropriate remedy is followed by a rapid symptomatic cure. This is a group of young adults of both sexes who present a low basal metabolism. In some of these young adults there are some of the usual symptoms of hypothy-

roidism Ordinarily, however, the only definite symptom besides that of the "cold" is loss of energy or, in the jargon of the young adult of today, "loss of pep"

The first patient, Mr P, is eighteen years of age The family history is essentially negative He had his tonsils removed at ten, his appendix, at fourteen When he was first seen on October 21, 1924 he gave a history that he had had a persistent sniffing cold and some cough since March, 1924 He spent the summer in the far West hoping to benefit this "cold," but there was no change even in the high dry air of Arizona or in California He had lost 10 pounds He was nervous and was unable to concentrate upon his work On physical examination there was found slight fulness of the thyroid gland An occasional râle was heard in the chest Otherwise the examination was negative The x-ray examination of his chest was negative He was referred to Dr G L Tobey, Jr, who reported that he found a chronic hypertrophic vasomotor rhinitis The nasal sinuses were clear and the nasopharynx showed the result of an almost perfect operation Dr Tobey was unable to find any definite focus of infection in the upper respiratory tract The condition of the upper air-passages at once suggested to Dr Tobey a vasomotor rhinitis associated with hypothyroidism The basal metabolism was done with some technical difficulty because the patient was very late to his appointment The basal metabolism reading was only approximate and was -5 per cent Because it was evident that the actual reading was unquestionably lower, he was at once started on thyroid substance, and within two weeks reported himself free from cough and with abundant energy However, this patient illustrates the fact that few of us are totally immune to upper respiratory infections, because he has since acquired an ordinary upper respiratory infection which has run the usual course The striking feature is that a condition that had been persistent for over six months, including the summer, could be promptly and completely relieved

The second patient is a young woman of twenty-nine, a stenographer Her family history is negative She had her

tonsils and adenoids removed at seven, and had some operation on her nose at twenty-three. When she was first seen, December 16, 1924, she gave a history of continuous sniffing cold since September, 1924. She had some cough and a little hoarseness, all of which were particularly distressing to her because she is an amateur singer of some ability. She said that for several years she has had an increasing number of minor colds both in the summer and in the winter. She has also gained some 40 pounds in weight in less than five years. Her menstruation has recently become scanty. On examination she weighed 156 pounds with her clothes on. She looks well and healthy. There is no focus of infection in her upper air-passages. The mucous membrane of the nose and throat was suggestive of hypertrophic vasomotor rhinitis. She has a slight thyroid enlargement. Her physical examination otherwise was negative. There was no x-ray examination of her lungs, but the clinical examination of her lungs was negative. Her basal metabolism was -18.7 per cent. On December 23, 1924 she was put on 3 grains of thyroid substance each day, and has been seen each week. Very promptly there was a marked amelioration of symptoms, both in regard to "colds" and in regard to her general condition. Today she reports that she has been having the "cold" which has prevailed in her office, but it does not seem to be the same kind of "cold" that she has had before. She reports that she is enthusiastic about her general condition. She has lost 7 pounds, partly attributable probably to the elimination of sugar from her diet.

These 2 illustrative cases are still taking thyroid in small amounts. The amount of thyroid that must be given is still problematic. The amount must be checked up (1) by repeated basal metabolism tests, (2) by the effect on the symptoms of vasomotor rhinitis, and (3) by careful scrutiny of possible symptoms of thyroid intoxication. It is too early to state how long thyroid substance will have to be administered. It seems likely that the derangement of the thyroid gland is temporary and not permanent. It is of some interest to speculate if the well-known favorable effect of potassium iodid and syrup of hydriodic

acid in some of these conditions is not due to the effect of the iodine on the thyroid gland and on the basal metabolism

It will be noted that both of these cases presented a slightly enlarged thyroid gland. That is not at all constant. In one patient the lungs were entirely clear, and the symptoms were apparently entirely confined to the nose and throat. In the other case there was also cough and presence of coarse râles, indicating that the process had extended to the larger bronchial tubes. It will be noted, furthermore, that one of these cases presented a sudden increase in weight and disturbances of the menstrual function without anemia, which also suggests thyroid disturbance. Such additional symptoms of hypothyroidism are, however, by no means constant. At the present time it is not possible to state exactly what is the mechanism of the underlying abnormal physiology. All that can be said is that there is a group of young adults of either sex who present vasomotor rhinitis with a low basal metabolism, and who seem to be symptomatically cured by the appropriate administration of thyroid substance.

There are, of course, serious difficulties in the administration of thyroid substance. This administration should be carefully done under very careful observation. An obvious additional difficulty presents itself, in that these patients are ordinarily ambulatory and busy with their usual occupations, so that the determination of the basal metabolism is not always easily fitted into their daily régimes.

Certainly thyroid substance is not to be promiscuously and casually given to all patients with persistent colds. It must first be determined that there is no source of infection in the upper air-passages. The competent nose and throat specialist now recognizes the typical appearance in the nose and throat. If, in addition, there is no evidence of tuberculosis, then only on the basis of a low metabolism rate is it permissible, in my opinion, to inaugurate thyroid therapy, which must be carefully observed.

Finally, I want to emphasize my belief that this group of cases is probably small.

CLINIC OF DR WILLIAM H ROBEY

HARVARD MEDICAL SCHOOL

THE DIFFERENTIATION BETWEEN GALL-BLADDER DISEASE AND CORONARY SCLEROSIS IN THE MIDDLE-AGED

IN this lecture we are not particularly concerned with well-defined cases of coronary thrombosis or gall-stones. Both may be characterized by collapse, by pain of excruciating intensity, and with similar distribution, although the pain of the former is more commonly in the precordium, often near the base of the heart and in the arm, while the pain of the latter is generally in the epigastrium and back. It was formerly thought that coronary thrombosis was always quickly fatal, but we know now that it is not always so, because the smaller the vessel involved, the greater the opportunity for at least temporary recovery. Hence, it may be mistaken in its mildest form for angina pectoris.

We are to consider, therefore, the differential diagnosis of two conditions, or their combination, which offers a puzzling question in hospital, but more often in private, practice. I refer to the milder attacks of pain in the epigastrium or precordium, and to the means at our disposal for the grouping of signs of gall-bladder disease and coronary sclerosis. I say more often in private practice, because these patients are frequently but mildly attacked, and seek advice during the intervals of reasonably good health. The history and signs may be so undefined as to necessitate seeing the patient during an attack, when that is possible, but even then there are often elements of doubt.

Youth is a helpful element in differentiating between gall-bladder disease and coronary sclerosis, since the former is many times commoner in youth than the latter. In Faulkner, Marble, and White's series at the Massachusetts General Hospital the

youngest patient with coronary occlusion was forty-two, while 12 with gall-stones were younger. The youngest patient I have seen with coronary occlusion was forty-seven, but I have seen repeated attacks of angina pectoris in a woman of nineteen with mitral stenosis, and in a man of twenty-one with aortic regurgitation. In the young with symptoms of angina pectoris there is generally some well-defined cardiac lesion, but in the middle-aged the diagnosis must frequently be made from a thorough history and the physical signs of arteriosclerosis. A combination of gall-bladder disease and coronary sclerosis would ordinarily occur only in the elderly.

Pain—In gall-bladder disease it is frequently in the epigastrium and may radiate to the back near the angle of the right scapula. It is rarely in the precordial area. Eating may bring on the pain, but it occurs without any relation to food. Exertion practically never induces an attack. In one case, which will be given later, the pain of gall-bladder disease came without apparent cause at intervals of several months, but angina pectoris was induced whenever there was undue exertion, although never after eating.

In coronary sclerosis the pain is usually precordial. It may rarely be epigastric. It may not amount to actual pain, but only to a sense of compression in the chest. In my experience it is often at the base of the heart. Unlike gall-bladder disease, it is frequently in the left arm. It may be in the left arm and not over the heart, or it may begin in the fingers, ascend the left arm, and end in the precordium. In but 1 case was there a complaint of severe pain in the back. That was a man of seventy-eight, who had angina pectoris with precordial pain, who later died of coronary occlusion. Frequently tender areas over the precordium are found. There may be simply attacks of numbness in the left arm without pain. Angina pectoris may be induced by mental or physical exertion, but it may, and often does, occur at night after several hours of sleep. I regard this as so important that I always enquire carefully into this part of the history.

Indigestion—In gall-bladder disease indigestion is common during an attack, often accompanied by nausea and vomiting,

but in the intervals there is also more or less indigestion, frequently unaffected by any form of diet or medicine. Even when the patient is living a most careful life in the effort to avoid attacks, he may be seized without apparent reason.

In coronary sclerosis the patient frequently seeks advice because of indigestion. He imagines that the pain in his heart is due to indigestion rather than the reverse. I have seen a number of such cases treated on this assumption without success, but if you have succeeded in making a diagnosis of coronary sclerosis and will give cardiac rest, you will see the indigestion disappear, often without any medication directed to the stomach. This reward is rarely similarly attained in gall-bladder disease. Nausea and vomiting are unusual accompaniments.

Jaundice may occur in any form of gall-bladder disease, but it is not seen in coronary sclerosis except in those unusual combinations of anginal and congestive heart disease.

Nitroglycerin or Amyl Nitrite—In doubtful cases a therapeutic diagnosis can sometimes be made by watching the immediate cessation of an attack of angina pectoris after the patient has chewed a fresh tablet of nitroglycerin or inhaled the fumes of amyl nitrite.

The Electrocardiogram—Willus has reported electrocardiographic studies in 155 cases of angina pectoris, in 11.6 per cent of which are found alterations in the T wave, but the findings of many other observers have not been so satisfactory. Even in coronary occlusion 9 cases of Longcope's proved by autopsy had inconclusive electrocardiograms, and while Faulkner, Marble, and White think they give suggestive evidence in favor of coronary occlusion when they show intraventricular block or changes in the T-wave in Lead II, they are by no means constant findings. It is a regret that this much help is not always present in such a difficult problem.

Diagnosis—In the diagnosis we have three conditions to determine: (1) gall-bladder disease, (2) coronary sclerosis, (3) gall-bladder disease and coronary sclerosis in the same patient. Naturally the history which we have outlined enters largely into the formation of an opinion.

1 *Gall-bladder Disease*—If the gall-bladder has been repeatedly inflamed it may be palpated through the abdominal wall, but often the examiner is disappointed. Frequently there is tenderness on pressure just under the ensiform. The subcostal part of the liver and the dorsal surface are often tender. The entire free border of the liver may be tender during an acute attack, but in the intervals the tenderness is limited to the neighborhood of the gall-bladder. Jaundice, while often absent, is a valuable sign, and its lightest shades should be carefully watched for. Radiographic studies are helpful in certain cases with stones, but the results are often disappointing, since even when stones are present the radiograms may be negative. Nevertheless, they should be taken in every case. Intercostal tenderness in the ninth, tenth, and eleventh right spaces is frequently elicited in cholelithiasis. The stools should be put through a sieve to find stones. Bile drainage has been thoroughly tried, but the amount of help received from the test is often very slight.

2 *Coronary Disease*—Occasionally the disease may exist without anything but the history of the attacks. Angina pectoris may be severe, followed by sweating and exhaustion, and yet there may be very few physical signs. Usually, however, there are sufficient to make the diagnosis. The heart may or may not show enlargement by percussion and fluoroscope, but the aorta frequently is increased. The radials are often thickened, and these alone, with the history of attacks induced by exertion, are enough to make the diagnosis in many cases. There is usually the soft-blowing systolic murmur in the aortic area, with accentuation of the aortic second sound. Frequently there is another soft systolic murmur in the cardiac impulse area. The diastolic blood-pressure is generally increased. In other words, there are many of the signs of arteriosclerosis. Once established, the attacks occur much more frequently than those of gall-bladder disease. At first only after undue exertion or sometimes a heavy meal, but as the sclerosis advances they become more frequent in spite of the greatest care. The patient is oppressed for breath and his face is pallid. One man told me

that he often had an attack when walking from the car to his house, and his wife could tell as soon as she saw him if he was having angina pectoris. Dyspnea occurs with only slight effort and the pulse is easily accelerated.

3 The Combination of Gall-bladder Disease and Coronary Sclerosis—The separation of the two requires a careful analysis of symptoms perhaps best illustrated by the recital of cases

Case I Gall-bladder Disease—Male, a plumber aged fifty-four

Family history unimportant

Past History—General health has been good. No rheumatic fever. Denies venereal disease. Acute appendix removed seven years ago. Head, eyes, ears and nose negative. No sore throats or tonsillitis. Teeth extracted for caries, except 5, which are not devitalized. Cardiorespiratory. No dyspnea, palpitation, or edema. Genito-urinary negative. No joint involvement or pains. Occupation, always a plumber since fourteen years old, for the last nine years has not done actual work and has not come in contact with lead to any extent in recent years. Weight Present 235 highest 267 lowest 230 pounds.

Present Illness—Onset eighteen years ago, with pain in right upper quadrant radiating to the precordium. It was a dull pain, unaccompanied by vomiting or jaundice. Occasionally nausea was a feature, as was pyrosis. Attacks lasted for about two to three weeks, and recurred at the beginning of the seasons. No radiation or numbness in the left arm. Occasionally some substernal tightness. These attacks were unaccompanied by dyspnea or fear of impending death. Usually occurred four hours after meals. Relief was occasionally obtained by food and soda. The course had been characterized by an increase in the severity of these attacks.

Physical Examination—Temperature 98.6° F, pulse, 80, respiration, 18, blood-pressure 145/90. Skin head, sinuses, eyes, ears and nose negative. Tonsils small and ragged. Teeth, all but 5 extracted, 2 of these carious. Glands negative. Heart

not enlarged and no murmurs Aortic second is accentuated Lungs negative Blood-vessels Radials are palpable, but not markedly thickened, pulse equal on both sides, rate 80, regular in force and rhythm Abdomen negative save for flabby wall Extremities negative Rectum negative Ophthalmoscopic Physiologic cupping, tortuous vessels Gastric analysis Ordinary curve, one-half hour free 10, total 23, one hour free 15, total 26, one and one half hours free 10, total 23 No occult blood x-Ray suggestive of a pathologic gall-bladder On May 17, 1924 a thickened gall-bladder, containing much fine gravel, removed Uneventful recovery In July, 1924 reported complete relief from symptoms

Opinion—From the history and physical examination he was believed to have cholecystitis, but relief by food suggested duodenal ulcer, while the radiation of pain and moderate arteriosclerosis made angina pectoris possible On August 11th he returned because of pyrosis and precordial pain without radiation, accentuation on exercise, or dyspnea Treatment with belladonna and alkaline powder gave complete relief On December 15, 1924 he was examined by the writer, who found the pulse-rate 96 and blood-pressure 138/90 He had been entirely free from symptoms

Case II Gall-bladder Disease—Woman, fifty years old, admitted to the Boston City Hospital January 21, 1924, discharged February 28, 1924

Family and past histories not remarkable

Present Illness—For four years has had dyspnea on exertion Eight months ago had a severe attack of pain beginning in the precordia and radiating down the left arm, which was diagnosed angina pectoris by her attending physician She stated later that just before the attack she had eaten inordinately of French pastry She belched considerable gas during, and some between, attacks Often there was pain in the back The face was red during an attack In November, 1923 x-ray plates showed a pathologic gall-bladder

Physical Examination—Obese, no pallor at any time, heart

rate 70 to 75, varies with respiration. The left border of the heart is 10 cm from midsternum. No murmurs, no special accentuation of the aortic second sound. There was a slight enlargement of the aorta. Blood-pressure 172/92. Urine negative. Phenolphthalein 40 per cent. Wassermann negative. Abdomen negative except for thick wall. No tenderness in gall-bladder region. The attacks of pain occurred every night, high up under the sternum and often radiating to the left arm. Nitroglycerin did not relieve.

We could not decide upon the diagnosis. We felt that she had angina pectoris, but were in doubt about the gall-bladder. The long history of dyspnea on exertion and the character of the pain suggested the former. On the other hand, there were few circulatory findings, no pallor, and the suggestive x-ray plates.

On March 25, 1924 Dr F H Lahey removed a "pathologic gall-bladder." Late in April her husband had an acute illness of several weeks, through which she nursed him and did the housework too, all without undue fatigue.

January 22, 1925. Since one month after operation the attacks suggesting coronary sclerosis ceased. Her only discomfort is a dull ache in chest when walking up grade, but never any sharp pain in precordia or arm. The pulse is 80 and the blood-pressure 140/100. It is probable that this patient has slight cardiac insufficiency, but the chief cause of pain originated in the gall-bladder.

Case III—Coronary Sclerosis—A canvasser, formerly a bartender and prize fighter, fifty-two years old, divorced.

Family History—Essentially negative. Wife is living and well, no miscarriages. Always taken coffee, tea, and alcohol freely. About 20 cigarettes daily. No drugs. Does not remember any childhood diseases. Rheumatic fever in 1904. A rare attack of tonsillitis, but never very ill. Generally healthy and a hard worker. Ears, nose, and teeth normal. Cataract in right eye discovered one year ago. Throat as above noted. Says he has had a systolic murmur for three years. Appetite

and digestion good Best weight 210 pounds (twelve years ago), present weight 176 Chancroid once, no history of lues

Present Illness — Onset one and one-half years ago Attacks of burning sensation, fulness in upper abdomen two to six hours after meals, not relieved by soda or food No nausea or vomiting For three or four months the pain has increased, has radiated to the right shoulder Morphine has been necessary There has also been radiation to the precordium and left arm The sensation down the left arm has been numbness rather than pain

Physical Examination — The examination negative save for cataract, a systolic murmur at the cardiac impulse area, and an accentuated aortic second sound No sclerosis Blood-pressure 155/80

A diagnosis of cholecystitis was made, but because of the precordial radiation angina pectoris was considered The patient had several attacks which were not relieved by nitrites, but were definitely relieved by morphine The pain on two occasions, though typically that of gall-bladder disease, was noteworthy because of the numbness down the left arm

x-Ray plates suggested a "pathologic gall-bladder" Blood, urine, gastric contents, and stools were negative At operation on April 17th a large thickened gall-bladder was found without any calculi His surgical convalescence was uneventful and there were no attacks of pain In June, August, and September he reported to the clinic that the pain in the upper right quadrant had ceased, but there was pain in the epigastrium and precordium, on exertion Rest and nitroglycerin relieved the attacks In August the nitroglycerin gave only temporary relief, so the sodium nitrite was added

January 15, 1925 Has very marked pain in epigastrium when walking only a short distance No pain in arm

This case illustrates one point we wish to emphasize When there is a strong suggestion of gall-bladder disease, even though angina pectoris is indicated, the patient should have the opportunity of recovery by operation You have seen the advantage of this in Case II Many middle-aged patients have some

pathology of the gall-bladder, and in Case III it had probably but little to do with the patient's attacks, yet operation gave him the benefit of the doubt. If he had both conditions as a cause of pain the order of importance had to be reversed after operation. One might think that the gall-bladder pain exceeded the angina pectoris, so that no relief was felt until morphin relieved the former. Angina pectoris is sometimes so severe that only morphin gives any comfort.

Case IV. Gall-bladder Disease and Coronary Sclerosis — A man, sixty-nine years of age, had for several years infrequent attacks of indigestion characterized by gas, distress after eating, and loss of appetite. In the spring of 1922, while in France, he had a longer and more severe attack, but no definite diagnosis was made. In October, 1922 he had another attack, in which the writer saw him. There was no temperature, no elevation of the pulse, but there was distinct tenderness upon pressure directly below the ensiform. The cardiac examination did not differ from that of many men of his age. His blood-pressure was within normal limits, there was a blowing systolic murmur over the aortic area, with slight accentuation of the aortic second sound, and the arteries were moderately sclerosed, but more important was his statement that for two years he had not been able to walk up a short incline from his office without dyspnea and a sense of constriction in the precordial area. He never had pain in any site. The Wassermann was negative and the non-protein nitrogen not remarkable.

With the cessation of the attack a bismuth series showed a pathologic gall-bladder, with a doubtful shadow of calculi. Since he was again as comfortable as ever, with fairly good digestion, he decided not to be operated upon. In September, after a satisfactory summer, he had another attack in which he was seen by a physician, who made a diagnosis of nervous indigestion. The writer saw him four days after the beginning of the attack, when there was a temperature and pulse of 100, with distinct tenderness over the gall-bladder and liver areas. The new and striking feature was a distinct jaundice of the scleræ and skin.

Operation was performed and a gall-bladder of about one third the normal size, free of stones, but with many adhesions, was removed. The gall-bladder did not look unlike the ordinary appendix. The patient made a satisfactory recovery except for a phlebitis in one leg. The cardiac condition was not altered during this period. Ten weeks after operation, when sitting at supper, he had hemiplegia with total aphasia. He regained sufficient power to walk unassisted and could say a few words. About three months later, while taking a few steps in the corridor of the hospital, he became dyspneic, cyanotic, and pulseless, his heart did not respond to stimulation, he lapsed into coma, and died in four hours.

Operation proved the gall-bladder diagnosis, but what about the coronary sclerosis? There was the suggestive history, always so important. The hemiplegia was, of course, of arterial origin, and death five months after operation was from coronary occlusion. The diagnoses were made fairly early and the course of events proved them. The separation of the two groups of symptoms was easier in this case than in some of the others. Attacks of compression in the chest with dyspnea came on principally with undue exertion and were unaccompanied by indigestion. The latter was fairly good except for certain irregular periods, when there was accompanying epigastric tenderness which generally persisted for at least a week, and during which there was no perceptible change in cardiac action or sufficiency.

I am indebted to Dr Percy B Davidson of the Boston City Hospital for the clinical data of Cases I and III.

CLINIC OF DR SAMUEL A LEVINE

PETER BENT BRIGHAM HOSPITAL

CASES OF CORONARY OCCLUSION, WITH RECOVERY

DURING the past few years there has been an unusual interest shown by the medical profession, and even by the laity, in the problem of angina pectoris and coronary disease. The cause of this unusual interest is twofold. In the first place, the medical profession has become more aware of the fact that heart disease in its various aspects is now the most important cause of death and morbidity with which we have to deal. This state of affairs is being emphasized through medical literature, and even by means of the lay press. It is gradually dawning on many physicians that angina pectoris is a common condition, is frequently overlooked, and is the cause of many fatalities that previously were not understood. In the second place, since the introduction by Jonnesco of surgical procedures that have attempted to relieve attacks of angina, the problem is no longer limited to the internists, but surgeons throughout the world have become more familiar with this cardiac disorder and have been trying to select the proper patients for cervical sympathectomy, which has given relief to a small number of patients that have been operated upon.

It may be proper at this point to say a few words about angina pectoris before taking up the main part of this clinic, which is to deal with cases of coronary occlusion with recovery. At present we are still somewhat in the dark as to the underlying cause of angina pectoris. In general, there are two points of view. The old one is that angina is caused by disease of the coronary vessels and that the attacks of pain are due to spasms of the vessels.

with temporary local or more general inanition of the heart muscle. The more recent point of view, particularly sponsored by Sir Clifford Allbutt, is that angina pectoris is always due to aortitis, sclerotic, luetic, or of some other nature, and that the condition of the coronaries is incidental. This latter hypothesis, if true, would readily explain those rare but apparently authentic instances of angina pectoris, in which careful examination at autopsy fails to reveal significant changes in the coronary vessels. From a practical point of view it seems to me that one might take the following attitude toward this question. It is reasonable to regard the individual attacks of angina as due to aortitis, the attacks themselves being precipitated by effort, chilling, etc., but that the length of life and general prognosis of the condition would depend upon the health of the coronary arteries. In other words, the transient or momentary attacks of chest discomfort which may go on for years may well be due to disease of the aorta. How long the patient is going to live will depend on whether the coronary vessels have remained patent throughout this time, whether there have been attacks of coronary occlusion, and what the likelihood of such catastrophes happening in the future. This viewpoint is borne out by the fact that, except for extremely rare instances, the patients who die of angina pectoris show that exitus follows occlusion of a coronary artery with resultant infarction of the heart.

A distinction between ordinary attacks of angina pectoris and attacks of coronary occlusion must be clearly borne in mind. The two conditions are different in many respects. The symptomatology and the physical findings are quite different. The treatment and prognosis are entirely different. In the selection of cases for sympathectomy it is of primary importance to distinguish one from the other, for, whereas there may be sound reasons for doing sympathectomy on patients with ordinary angina pectoris, it seems to me that it would be worthless to try this procedure with those who have had attacks of coronary occlusion, for in the latter cases the structural damage to the heart itself is too profound to warrant an operation, which at present, at least, seems only to be palliative.

Let us, therefore, first picture an attack of angina pectoris so that we might be able to compare this with a similar picture when the coronary vessel is occluded. The ordinary anginal patient is a man fifty odd years old, who previously had been very well and usually strong physically, and even of the muscular and robust type. There often will be a family history of vascular disease of one kind or another. In the past history infections play an insignificant rôle. A small number of them may have had diabetes, syphilis, gout, or chronic lead-poisoning. The past history of rheumatic fever is unimportant, although occasionally there has been evident rheumatic aortic insufficiency. Preceding mitral endocarditis is very rare indeed. In general one might say that the majority of cases come without any specific etiologic factor. In fact, even hypertension is by no means a constant concomitant of angina. The blood-pressure may be anywhere from normal or subnormal to one that is extremely elevated. The average systolic pressure of over 100 cases of angina pectoris I found to be 160 systolic and 95 diastolic. Sclerosis of the peripheral radial and brachial arteries would be marked, moderate, or absent. From the above we can see there is no constant finding in the background that would help in the diagnosis.

Of much greater importance is the type of symptoms of which the patient complains. It is of much greater value to inquire carefully into the symptoms of the patient than to perform any special test that is now known. The primary complaint is a feeling of constriction, or pressure, or fulness, or tightness, or pain in the center of the upper portion of the sternum. It is important to bear in mind that anginal pain is only rarely apical. The pain below the left breast or around the nipple region is much more associated with functional cardiac disorders, valve disease, or chronic myocarditis, than it is with angina pectoris. The typical sternal distress in most instances is brought on by effort, especially on walking up a little grade or against a cold wind. Effort combined with a full stomach is borne less easily than otherwise. The constriction or pain in the chest need not radiate at all, although in many it spreads to the left shoulder.

and down the left arm. Sometimes it goes to the right arm or to both arms, and the pain may begin in the arms. When an attack comes the patient will state that he becomes immobile, does not want to walk or move, and on resting the discomfort gradually passes away in a few minutes. Similar relief follows administration of nitrites. Should you be fortunate enough to see the patient during an attack, you will find that the pulse-rate remains unchanged, or rises slightly, and the rhythm remains normal. If you had the opportunity of making blood-pressure readings at this time, you would generally find that the systolic pressure would rise during the spell 20 to 50 mm., and would fall back to its normal level as the attacks subside. The expression on the patient's face would be somewhat set and apprehensive and he might appear a little pale. In many instances there is no sense of impending death, this varies considerably, depending a great deal on the severity of the attack, the previous frequency, and the general psyche of the individual. After the distress has disappeared in most instances the patients feel quite normal. They may continue to enjoy good health in the interim.

The reason that many patients and some physicians overlook these symptoms is because they often create the impression in both the patient's and the physician's mind that the whole affair is "just a little indigestion!" The reason for this attitude is that the patient will often experience relief when he finds it possible to raise a little gas from his stomach. He may insist that he has no pain, but merely experiences a fulness behind his sternum, and that if he could only raise up some wind this feeling of pressure would disappear. We must, however, be on our guard for any feeling of indigestion that comes on following effort. If we keep this in mind, we will properly diagnose many such cases, and there will be fewer patients reported as dying of acute indigestion. I believe that we will be closer to the truth if we hold that all patients who die suddenly of acute indigestion suffered from angina pectoris and the accompanying coronary sclerosis. In the milder form of this complaint the true state of affairs can only be elicited by the most careful questioning. When I say mild form I merely mean that the symptoms may be

mild Whenever the diagnosis of angina is made, the severity of the disease and the general prognosis does not necessarily depend upon the degree of discomfort that the patient has had, but upon your general estimate as to the health of the coronary vessels A patient who walks into your office complaining of only mild sternal distress may be dead within a week, for, although the symptom is mild, the condition is grave

Let us now contrast the above with the findings that are presented when a patient has an attack of coronary occlusion Let us picture a man of fifty-five, looking strong, muscular, well for many years, who has for the previous year complained of a little tightness in his chest on hurrying Either after some effort like walking on a golf course, or even while perfectly quiet in bed, he is taken with a very severe attack of pain in the center of his chest, crushing in character, with or without the customary radiation He quickly knows that this attack is different from any he has ever had He becomes prostrated, may actually faint, but is more apt to be in a state of moderate collapse or shock. He becomes pale and ashen in appearance and cold perspiration breaks out on his skin The customary relief that he previously experienced from nitroglycerin is not obtained even if several tablets are taken Amyl nitrite, if tried, fails to give him relief The physician is apt to give morphin, but it is astounding that $\frac{1}{2}$ grain or more may only diminish the discomfort slightly The pain, instead of letting up in minutes, will last for hours or a day or more

Let us assume that we know the previous blood-pressure of this patient to have been 180 mm systolic During the course of the first several hours following the attack a fall in pressure would be noted This may be sudden or gradual When first seen the reading might already be 120, and later it may fall to as low as 90 In other words, with this attack there has been a marked fall in pressure, while during the attacks of ordinary angina pectoris the pressure, although occasionally remaining unchanged, is much more apt to rise during the attack Another important difference is in the actual heart rate After the attack of coronary occlusion the heart rate would be found to be accel-

ated, and it will remain constantly rapid for some days, from 90 to 120. With the ordinary anginal attack the rate is more likely to be slow, around 70 per minute. The pulse is small and thready. Listening over the heart the sounds have a tic-tac quality or are very distant. Not infrequently the first heart sound at the apex is practically or completely inaudible. At times a gallop rhythm will be heard. This again is in striking contrast to the auscultatory findings in ordinary angina, where the heart sounds may be essentially normal. Examination of the lungs in most instances shows the presence of râles at the bases of the lungs, and occasionally there may be evidence of generalized edema of the lungs. The liver, in the course of a short time, may become engorged and even tender. The following day the blood may show a considerable leukocytosis, from 15,000 to 30,000 white cells. A temperature of 100° or 101° F is generally found. A slight icteric tint may be present in the sclera as the result of the hepatic congestion.

At this point it is well to bear in mind that the entire picture may simulate that of acute surgical abdomen, for, not infrequently, the fulminating pain is located not in the chest, but in the upper abdomen, like that seen in an acute pancreatitis, ruptured gastric ulcer, or gall-stone colic. There may be, in addition, nausea and vomiting. The differential diagnosis becomes particularly important when you recall that a leukocytosis and a temperature of 101° F or thereabouts often develops as a result of infarction of the heart. These findings, together with spasm, tenderness, and pain in the upper abdomen, the questionable jaundice, and the shock, all fit in so well with the diagnosis of acute surgical abdomen that occasionally these patients are operated upon by mistake.

There are a series of events that may develop following such an attack. Death may be instantaneous or come within several hours, or the patient may hover in rather a desperate condition, but gradually improve. At a moment when you think the patient is no longer in danger, even when all symptoms have disappeared, sudden death may ensue. When we keep in mind the pathologic changes taking place in the part of the heart muscle that was sup-

phed by the occluded coronary artery we can readily understand the events that are being detailed. The infarcted area may soften, and although the circulation seems to be doing satisfactorily, sudden exitus may occur in the second week of this illness. The cause of sudden death coming at this time is a rupture of the infarct, with resulting hemopericardium. The internal surface of the ventricle (it is almost always the left ventricle) underlying the infarcted area develops a mural thrombus. If the thrombus remains adherent and firm, at least temporary recovery can take place. Parts of this thrombus, however, frequently become dislodged and result in hemiplegia or emboli of the peripheral organs. The process may extend over the infarcted area outwardly and involve the pericardium. When this happens over the anterior portion of the heart a localized pericardial friction-rub may be heard. This, when present, we generally find during the first few days. Under favorable circumstances healing of the entire injury may occur, with complete recovery of the circulation. It is especially with this latter group of patients that I am concerned in this discussion, and I want to emphasize that there are numerous instances of infarction of the heart following coronary occlusion that result in recovery and that the patient often returns to fairly active life for some years. It is because of this possibility that the care of patients suffering from coronary occlusion demands our most careful attention, for the difference between proper and improper treatment may mean the difference between death and some years of usefulness.

Case I—The patient was a man of fifty. He had always been well, strong, and vigorous working very hard, and indulging in a great deal of strenuous physical exercise. Two years before he was first seen he had a violent streptococcus infection of the hand and was extremely sick in bed for ten weeks. On April 7, 1923 he was awakened from sleep with pain in the lower sternum, which did not radiate. The pain was of a pressure character and lasted about half an hour. It subsided just before morphin was to be given by his physician. After that

there were several shorter and milder attacks, coming without effort. He felt that eructation of gas would give him relief from this discomfort. There never was any indication of dyspnea in the past history and there was none associated with this attack.

Examination that forenoon showed a vigorous, plethoric looking individual. The blood-pressure was 180 systolic, 110 diastolic. No pulsus alternans. The heart was not enlarged, left border, by percussion and palpation, 13.5 cm. to the left of the midline, right border 4 cm. to the right. Heart action was regular, 90 to the minute. The first sound was of good quality. No murmurs were present. The aortic second sound was slightly accentuated and there was no gallop rhythm. The lungs were clear throughout. The liver was not enlarged or tender. There was no peripheral edema. The radial and brachial arteries were slightly sclerosed. The urine examination was as follows: Yellow, clear, acid, specific gravity 1018, very slight trace of albumin, and no sugar. The sediment showed numerous white blood-cells and no casts. Electrocardiograms taken that morning showed a normal heart mechanism. There was evidence of considerable left ventricular hypertrophy, but the ventricular complexes were essentially normal. The T waves were upright in all leads. He was considered to have angina pectoris and was told to go to bed, to reduce his weight, and to diminish his salt and protein intake in his food. Nitroglycerin was to be used freely for attacks of chest pain.

Two days later he was taken with violent clutching pain in the manubrium, lasting from 9 P. M. to 2:30 A. M. During this spell he received five subcutaneous injections of 15 mgm. of morphin sulphate. Nitroglycerin was tried at this time, but gave no relief whatever. He presented the appearance of collapse. He perspired profusely and was very pale. The pulse was small, rapid, and regular, 120 to 130 to the minute. After 2:30 A. M. the severe pain subsided, but there remained an ache in the chest and the patient slept in short naps. Twenty-four hours later he was much better, the color had improved, but the pulse remained small, rapid, and regular, 120 to the minute. At this time a temperature of 100° F. developed, which

persisted for forty-eight hours, and there was an occasional extrasystole heard on auscultation over the apex. A week after the attack the pulse was still rapid and regular, 110 to the minute. At no time was a pericardial friction-rub heard.

On April 16th he had a severe pain in the left flank, radiating to the left leg and slightly to the genitals. It was sudden in onset, without any abdominal distention or discomfort. The pain lasted two days and then passed away. At this time the urine showed a great many red blood-cells and a rare cast. From then until April 25th the patient seemed to be doing satisfactorily, but on this latter day he had an attack of marked collapse and was almost pulseless. The body was cold and he presented a picture of profound shock. There was no pain associated with this spell, but a sensation of extreme weakness. After this he fell asleep, and on the next day was much better. From then on he steadily improved. He was kept perfectly quiet in bed until June 7, 1923. During all this time the heart sounds were somewhat distant, but there never were any murmurs. The patient was slowly allowed to get out of bed and he gradually returned to his normal activities. For the past one and one-half years he has been practically free from symptoms, and now for twelve months has been constantly at work, although he does not undertake as much as formerly. At present examination shows almost identical findings in the heart as compared to those present before the attack except that the heart sounds are slightly more distant. Blood-pressure is now 130 systolic, 85 diastolic. Electrocardiograms taken June 1924 show a change from an upright to an inverted T wave in Lead 1. The amplitude of the initial phase of the ventricular complexes is smaller in all leads than they were before the attack of coronary closure.

Discussion —It is perfectly clear that this patient was suffering from angina pectoris and that two days after he was first seen he had an attack of occlusion of the coronary vessel, with the resulting infarction of the left ventricle. The increase in pulse-rate, the fever, the failure of the pain to respond to nitroglycerin, and even to morphin, the decided fall in blood-pressure,

the long duration of the pain, all point to coronary closure and not to an ordinary attack of angina pectoris. Seven days after the attack, when pain developed in the left flank, associated with hematuria, an infarct of the left kidney must have taken place. This is readily explained when we think of the pathology that is going on inside the heart. A thrombus forms within the cavity of the left ventricle at the side of the infarcted area in the heart, and emboli may result from bits of tissue that can easily free themselves from this thrombus. It is somewhat a matter of chance as to whether such emboli eventually occlude cerebral vessels with resulting paralyses, or arteries in the limbs that may produce dry gangrene, or whether they localize in the internal organs. It is interesting that as recovery took place the patient thereafter maintained a lower systolic blood-pressure than before the attack, in fact, for a year and a half, it has never been higher than 130, whereas, previously, it was found to be 180. Another significant change was that seen in the electrocardiograms. The T waves, which previously were upright in all leads, are now directed downward in Lead 1, and the initial ventricular deflections (QRS waves) are now smaller in all leads than before the attack. As the patient was in his home during the acute illness, no tracings were obtained at the critical stage of the disease. It is important to bear in mind that this patient has been in excellent health following this attack, working all the time, and is free from anginal symptoms, probably because the heart now maintains a lowered blood-pressure.

Case II—The patient is a man aged forty-three, who was first seen June 3, 1923. He complained of substernal distress of a few months' duration.

Family History—Father died at seventy of angina pectoris. There were several aunts, uncles, and grandparents who had vascular disease and died of shock.

Past History—The patient has always been well, strong, and very active. He was always athletic and both played and worked very hard. There were no important acute infections.

Present Illness—For several months the patient had not felt

quite right. He tired easily and noticed some shortness of breath. In February, 1923 he developed a neuritis of the right shoulder and arm, which was very troublesome and lasted about two months. For two months he noticed a slight uncomfortable feeling below the upper sternum, coming on after effort. In May, 1923 his systolic blood-pressure was found to be 180. At that time the heart sounds were normal and there was a slight blowing systolic murmur all over the precordium. The urine was negative. Although he rested during the entire month of May, he still was troubled with a moderate amount of dyspnea and substernal constriction on walking. The sternal distress would always be relieved by taking nitroglycerin. On June 3d, when I first saw him, examination of the patient was entirely negative except for the findings noted above. A systolic murmur was heard all over the precordium. Blood-pressure was 160 systolic, 100 diastolic. The heart rate was between 60 and 70 and was perfectly regular. The vital capacity of the lungs was 3300 c c, and the electrocardiograms were essentially normal in every respect. He was put to bed for absolute rest and placed on Karel diet for a few days. This was increased to "light diet" thereafter. The following ten days he received 1/10 gram digitalis three times a day. Later diuretin, 3/10 gram, three times a day was also given. Despite the fact that he was constantly in bed he continued to have a slight uncomfortable feeling in the sternum not unlike those that previously came on after effort. The pulse was constantly regular, about 70 to the minute, and the blood-pressure fell to 142 systolic and 95 diastolic.

On June 24, 1923, at 5 30 P M, he was suddenly taken with a terrific attack of substernal clutching pain, which radiated to both arms. This was accompanied by pallor, cold sweat, and the appearance of shock. He was given four tablets, 1/100 gram of nitroglycerin, in quick succession, without any effect, 15 mgm of morphin were given subcutaneously, and in about three-quarters of an hour the pain subsided slightly. The heart became somewhat irregular, but the exact type of irregularity remained obscure. About one hour later the pain increased, and

another dose of 15 mgm of morphin was given. He became drowsy and slept in naps. At 10 P M a third dose of 15 mgm was given. At 8 P M the heart rate was 84 and there were occasional extrasystoles. The sounds of the heart were of fair quality. At 10 30 P M the rate rose to 114.

The following day the general appearance of the patient seemed poor. He vomited several times. The heart rate ranged between 110 and 120. The white count of the blood was 15,400. On the evening of the 25th the temperature rose to 99.2° F. The patient felt extremely weak and had a very anxious appearance. During the day he had to be catheterized, and in the evening a distinct gallop rhythm was heard at the apex. On June 26th the patient complained of some dyspnea. The respiratory rate was around 30 and periodic. The heart rate was 114 to 128. He complained of distress below the right costal margin. His liver was just palpable and tender to pressure. There was definite Cheyne-Stokes' breathing. No pericardial or pleural friction-rub could be heard. The heart sounds were distinctly more distant. He complained of slight distress around the apex of the heart, which was not relieved by nitroglycerin, in fact, the only medication which seemed of much use was morphin. At various times the heart rhythm was found to be irregular. There were sudden changes in the rate, due to short runs of rapid, irregular beats. On June 29th the Cheyne-Stokes' breathing was still found to be present. There had been considerable abdominal distress and during that day the patient was quite irrational. The heart showed signs of partial block with sudden changes in rate, from 86 to 130 or 140. The following day more marked sudden changes in rate were noted, 58 to 128, from minute to minute.

During the first week in July the patient slowly improved in general appearance, although frequent irregularities in the heart mechanism were noted. The systolic murmur, which had become practically inaudible during the early days of this attack, became louder and louder. At no time was a pericardial friction-rub heard. Frequently the heart sounds had a definite gallop rhythm. The temperature rose to 100° F on June 26th and

remained around 100 \pm ° F for a few days thereafter, gradually returning to normal around July 5th. On this latter day the pulse was 90 and a week later it averaged 80. During the first week following the severe attack of collapse there was a good deal of difficulty with the bowels, distention was most troublesome. This gradually cleared up. The blood-pressure which was around 140 systolic before the attack, was found to be 95 systolic and 75 diastolic on June 27th. During the following three weeks it slowly rose and averaged toward the end around 104 systolic and 65 diastolic. The systolic murmur became more audible and was heard both at the apex and the base. The patient gradually became free from all chest distress and no longer complained of dyspnea. He remained in bed for eight weeks after the attack and then was gradually allowed to get up.

In the fall of 1923 he resumed his ordinary activities, although he has never been able to work as hard as formerly. He becomes more easily short of breath. He definitely states that he has never had any sternal oppression during the year and a half since he left the hospital. He notices an occasional skipping of the heart-beat and a fluttering sensation over the precordium. He has taken no medicine; his strength has gradually increased, so that at present he plays nine holes of golf without any appreciable distress. On December 10, 1924 the blood-pressure was found to be 122 systolic and 84 diastolic. The vital capacity of the lungs was 2850 c c. The heart was slightly enlarged 12 cm. to the left of the midline, 1 cm. outside the nipple. Action was regular, 78 to the minute. Heart sounds were definitely distant. The first sound at the apex was particularly muffled. There was a faint systolic murmur at the apex. There was no gallop rhythm and no pulsus alternans. There were no signs of congestion in the lungs, liver or extremities.

The electrocardiograms went through some very interesting changes. They were essentially normal on June 1, 1923. This was before the attack. On June 28th, four days after the attack, they showed a slight delayed conduction of impulses from auricle to ventricle. This was at the time partial heart-

block was occasionally detected on auscultation. The amplitude of the initial phase of the ventricular complex (QRS waves) became diminished in all three leads. The T waves were diminished in height in Lead 1 and became inverted in Leads 2 and 3. On October 10, 1923 the electrocardiograms showed further changes. The amplitude of the QRS waves became still smaller. Since then repeated tracings show a gradual improvement, in that now (December 5, 1924) the T waves have become again upright in Leads 2 and 3, although in Lead 1 they are still slightly depressed, whereas in the original tracing they were upright.

Discussion—This patient had typical angina pectoris. On June 24th he suddenly had an attack of coronary occlusion with infarct of the heart. Most of the characteristic features were displayed and in many respects were identical to those described and discussed in Case I. Here the heart irregularity that developed shortly after the attack was due both to extrasystoles and partial heart-block, whereas in Case I only extrasystoles were noted. I have seen one instance of complete heart-block with a ventricular rate of 28 in a fatal case of this disorder. In Case II there was no evidence of embolic phenomena. This case also illustrates that recovery may be very satisfactory even after such a grave illness, and that with a lowered blood-pressure the patient may remain free from typical anginal attacks.

Case III—The patient is a business man, aged forty-three, whose main complaint when first seen (March 23, 1924) was pain in the center of the chest and left arm.

Present Illness—Until a few days ago the patient was in excellent health. He had never noticed dyspnea on exertion or any discomfort in his chest. He has been recently playing 36 holes of golf daily without discomfort. Two days before he was first seen, after a brief, quick walk, he suddenly began to perspire and felt a severe pain at the apex of his heart, which continued for a half-hour. He got a taxicab and returned home from his office. The pain was slightly relieved by rubbing the epigastrium. At this time there was no feeling of tightness.

He took a drink of whisky and belched up a good deal of gas. One-half hour later he vomited and the pain was relieved. After this there was a feeling of pressure under the sternum as if there was a ball of gas there that could not get up or down. On reaching home there developed a rheumatic pain the left arm. The pressure pain in the chest and arm lasted continuously for eight to ten hours. The pain in the chest disappeared before it did in the arm. The following day he vomited twice and all day he felt rather weak. Nitroglycerin did not relieve the pain, and it was necessary to give him two injections of $\frac{1}{4}$ grain morphin. The day following the attack his temperature was 100.6° F and the pulse was 110. During this day he had a short attack of auricular fibrillation, lasting about one hour. Previous to this the heart was regular, with an occasional extrasystole. The blood-pressure on the first day of the attack was 130 systolic and the next day it was 118 systolic.

Past History—No previous history of pneumonia, typhoid fever, rheumatic fever, or chorea. No past operations. He has always been a big eater. His weight has been constantly at 175 pounds.

Family History—One uncle died of angina pectoris. One aunt has marked vascular hypertension. Mother is living at the age of sixty-five and has marked arteriosclerosis. Father died at fifty of pulmonary tuberculosis, but had extreme arteriosclerosis for years before he died.

Physical examination March 23, 1924, two days after the attack. Blood-pressure was 112 systolic, 84 diastolic. Pulse, 114. Temperature 99.6° F. The patient was lying flat in bed somewhat apprehensive. The lungs were normal throughout. The abdomen showed no masses or tenderness. The liver and spleen were not felt. The heart was not enlarged on percussion. Left border 12 cm. to the left of the midline. Action was regular. An occasional premature beat was present. There was no gallop rhythm. There were no murmurs. No pericardial friction-rub could be made out. There was no pulsus alternans. There was no peripheral edema. At this time the patient was complaining very little. He looked slightly pale otherwise there

was nothing very striking on examination. On the following day the pulse was 108, temperature 99.6° F, blood-pressure 112 systolic, 78 diastolic, and there was a definite pulsus alternans. A presystolic gallop rhythm could be heard over the precordium. The white blood-count was 16,800 cells. The urine was amber, turbid, acid, specific gravity 1020, slightest possible trace of albumin, and no sugar. Sediment showed an occasional hyaline cast. He had a fair night and really felt quite well. In three days the temperature reached normal and the pulse gradually fell to 80. Respiration was not significant. He was kept absolutely flat in bed, receiving morphin freely to keep him quiet. After several days this was changed to veronal. The blood-pressure fell gradually during the first week to 94 systolic, 68 diastolic. During the following month this slowly rose to 110 systolic, 75 diastolic. At no time was a pericardial friction-rub ever heard. The gallop rhythm, which previously was quite definite, disappeared, and the pulsus alternans also disappeared as the heart rate slowed. The phthalein kidney function test showed 85 per cent excretion on October 16th. At this time the urine showed a rare hyaline and fine and coarse brown granular cast, also a rare white and red blood-cell. He was given diuretin 0.5 gram twice a day, from October 12th to the 18th. A possible difficulty with the bowels was anticipated by giving him liquid petrolatum, 15 c c every night and 5 to 10 c c of fluid extract of cascara every morning.

Electrocardiograms taken March 24, 1924, the day he came into the hospital, were normal except that the T waves began on the down stroke of the R wave at a point before it reached the base line. This is the type of change in electrocardiograms which occurs early in infarction of the heart, and which, when present, is a valuable point in the diagnosis. One week later the curves had changed so that the T waves were sharply inverted in Lead 1 and upright in the other two leads. Electrocardiograms, repeated April 17, 1924, were essentially the same as these latter ones. August 7, 1924 further electrocardiograms were taken and showed further changes. The T waves in Lead 1 again became slightly upright. The T waves in the

other leads were also upright. The last heart tracing, taken December 5, 1924 showed beginning signs of left ventricular preponderance which previously were absent

The patient was kept in bed for about two months and gradually allowed to resume activities. For the last seven months he has been attending to his business constantly and has been essentially free from pain in the chest. There has also been no dyspnea. He has taken practically no medicine and feels quite well, and in addition to his routine office work he plays nine to eighteen holes of golf rather frequently. During the past six months the first heart sound as heard at the apex has diminished slightly in intensity. A moderately loud systolic murmur has gradually developed at the apex. The blood-pressure on December 5, 1924 was 128 systolic, 90 diastolic. No gallop rhythm or pulsus alternans could be made out. Vital capacity of the lungs was 3750 c c.

Discussion—It is perfectly clear that on March 22d the patient had an attack of coronary closure, with resulting infarct of the heart. The picture in this case, as in the previous two, is quite typical. The chest pain lasted for twelve hours. It did not respond to nitroglycerin. A gradual fall in blood-pressure took place from 130 to 94, a slight fever and leukocytosis developed, and the electrocardiograms showed the changes that are rather characteristic of this condition. Nausea and vomiting occurred during the first few days of the illness, and it is well to remember that these and even more striking abdominal features are not at all rare, and should be properly appraised in patients where the question of surgical exploration for an acute surgical abdomen is being considered. One unusual feature in this case is the absence of a preceding history of angina pectoris, for only rarely is infarction of the heart the first indication that the patient has serious heart disease. It is also interesting that this patient has remained free from chest pain ever since the attack and symptomatically has done very well. At present he considers himself in excellent health.

Case IV—The patient is a clergyman, aged forty-nine, first

seen June 22, 1924 His main complaint was pain in the sternum

Present Illness—Twenty-eight hours before being seen the patient was taken with a peculiar feeling in both nipples This awoke him from sleep He tried to walk it off, but without success He could not eat his breakfast On getting up and about that morning the pain grew worse, and at 1 P M that day he was in such discomfort he could not take his clothes off He felt cold and clammy, but yet was walking around, $\frac{1}{100}$ grain of nitroglycerin was given under the tongue at this time, with considerable relief, but one-half hour later the pain returned as severely as ever Another $\frac{1}{50}$ grain of nitroglycerin gave slight relief, but again the pain returned During the afternoon he vomited This time he received $\frac{1}{2}$ grain morphin and 3 doses of $\frac{1}{8}$ grain each during that day About twelve hours after the attack began the pain let up completely, and there only remained a slight sense of soreness He slept from 11 P M to 4 A M that first night

The past history was unimportant as far as acute infections were concerned The patient was always a vigorous and plethoric type of individual On careful questioning it was learned that for several months he noticed a grasping and constricting feeling in the midsternal region on hurrying and on climbing stairs

On examination at 2 P M on June 22, 1924, that is twenty-eight hours after the onset of this attack, he was found lying flat and comfortable in bed without any apparent distress There was a little aching sensation in the center of the sternum Examination of the heart showed almost inaudible heart sounds The rate was 127 and regular Abdominal examination was entirely negative There was no liver tenderness There was a definite gallop rhythm The size of the heart was not well made out No apex impulse could be felt, No murmurs were heard Blood-pressure at this time was 140 systolic, 108 diastolic The day previous it was 160 systolic, 110 diastolic, and one year before it was 170 systolic and 130 diastolic The lungs were clear throughout There was no peripheral edema No pulsus alternans was made out Temperature 101.8°F rectally

On the following day the white blood-count was 30,000 Urine specific gravity 1027, acid trace of sugar, and a slight trace of albumin Sediment showed many leukocytes, a few fine granular and hyaline casts and a few fresh red blood-cells Bile was absent

The patient was diagnosed as having infarct of the heart with coronary occlusion, and was treated with absolute rest Morphine was given liberally, but no digitalis was used He remained free from pain The pulse-rate continued around 120 for about six days, although occasionally rates of 55 to 60 were observed It is quite possible that at this time the patient was having a two-to-one heart-block or extrasystole coming every second beat that did not reach the wrist During the following week the pulse gradually slowed to 80 or 90 There was an irregular fever ranging from 99° to 102° F during the first ten days, which gradually quieted down Two days after the attack a typical pericardial friction-rub was heard over the midsternum, not particularly well heard at the apex On June 28th the pericardial friction-rub was still present The heart rate was in the vicinity of 120 and a faint systolic murmur was heard at the apex No pulsus alternans A moderate number of râles were heard at the base of the right lung The blood-pressure, which previously was 140 systolic, 108 diastolic, gradually fell to as low as 90 systolic on the 25th and 26th, then rose to 114 systolic, 92 diastolic on June 28th The urine continued to show the slightest possible trace of albumin, normal concentration, an occasional hyaline and granular cast, with frequent leukocytes and rare red cells The sugar in the urine which was present at the beginning disappeared

When he was seen on July 28th, that is, five weeks after the attack, he had been in bed all this time and was feeling quite well The blood-pressure was 110 systolic and 90 diastolic The heart sounds were quite distant No pericardial friction-rub was present There was a definite constant trigeminy, every third beat being an extrasystole The patient remained under complete rest in bed for eight weeks and then was gradually allowed to get up He had an uninterrupted convales-

cence, felt quite well all this time, and on October 3d he was walking an hour at a time, showing no discomfort or fatigue. There had been no chest pain whatever. Physical examination on this day showed blood-pressure 124 systolic, 86 diastolic. The heart was made out slightly enlarged, 1 cm. outside the nipple. The apex impulse, which could not be felt, was now present, but feeble. The heart rate was 88, action absolutely regular. Sounds were almost inaudible. The first heart sound could not be heard at all, either at the base or at the apex, with the patient lying down or sitting upright. No murmurs could be heard. Lungs were clear. There was no edema. No pulsus alternans. The vital capacity of the lungs was 4300 c.c. Weight 201 pounds. Height 6 ft. Electrocardiograms, which were taken at this time and which were the only ones obtained, showed one striking feature. The ventricular complexes in all three leads were unusually small in amplitude. Similar curves I have noticed in several other patients who have come to autopsy and showed occlusion of the coronary artery with infarct of the heart. Up to the present time the patient has remained free from symptoms and feels almost as well as normally.

Discussion—The course that this patient ran is also quite typical of infarct of the heart. There was a marked fall in blood-pressure from the previous normal level of 170 systolic to 90 as a result of the attack, followed by a slow recovery to 110. The temperature, the elevation of pulse-rate, and pericardial friction-rub, and white count are all characteristic of this syndrome. In this case irregularity of the heart beat in the nature of frequent extrasystoles also developed. Sugar was found in the urine during the first few days of the attack. This feature has been noted in several other similar cases, occasionally in appreciable amounts, but always was transitory. It was first considered by his physicians that this attack was the first evidence of vascular disease, but on careful questioning a typical story of angina pectoris of three months' duration was elicited. The patient has remained free from sternal oppression, which was present for several months before the attack, ever since. This probably is related to the fact that he now carries a lower

blood-pressure The recovery has been most satisfactory in every respect

Case V—The patient was a salesman aged thirty-six His chief complaint was pain in the heart

Present Illness—Five years ago he had an attack like the present one only much milder Since then there have been occasional spells of chest distress, coming on after sudden effort like lifting or running He was first seen July 31 1924 Three days previously, while reading a paper, he was suddenly taken with an agonizing pain which started near the left nipple and spread to both shoulders and arms He felt as if something were gripping his heart This pain lasted five hours until morphin was administered The patient described the pain as having been "terrible" For three days following this the pain was still present, although much milder He had not slept for three nights At the onset he became wringing wet with the agony of the attack, and he thought that his end had come During the day he vomited once without relief

Past History—During his youth he had pneumonia typhoid fever, and malaria No rheumatic fever or chorea He had Neisserian infection many years ago

Family History—Mother died at forty-nine of cancer of the uterus Father died at fifty-one of influenza One brother and sister living and well None dead Wife living and well No children

Physical Examination (July 31 1924)—The patient was well developed Weight 160 pounds height 5 feet 10 inches Pupils equal circular and react normally Pulses were equal Lungs were normal throughout Abdomen was negative No peripheral edema Deep reflexes were normal The heart was not enlarged The action was regular No murmurs were present No pulsations were seen at the base of the heart Blood-pressure 100 systolic, 75 diastolic Temperature 99.8° F Pulse 96 Peripheral arteries not sclerosed Vital capacity of the lungs was 3850 c c The patient had to walk to the office for this examination where electrocardiograms were taken

They were fairly characteristic of infarct of the heart. The T waves in Lead 1 rose from the QRS complex at a point 3 mm above the base line.

The patient was sent to the hospital for a complete rest in bed. There it was found that the Wassermann reaction was positive, and x-ray examination of the heart showed some enlargement of the first portion of the aorta, extending backward, which appeared to be almost a sacculation. The patient was regarded as suffering from luetic aortitis and infarct of the heart from coronary occlusion. The pain quickly disappeared during the first few days of rest and the blood-pressure continued low. It was constantly at the level of 110 systolic and 70 diastolic. He was given potassium iodid and mercury, first intramuscularly and later in the form of blue mass, which was rubbed daily over various parts of the body. There was a slight temperature of about 100° F for a few days, and this gradually disappeared. The pulse-rate fell from 100 to the vicinity of 70, and the white blood-count, which was 14,500 on admission to the hospital, returned to normal. A lumbar puncture was done September 3d. This was found to be normal.

Repeated electrocardiograms showed the peculiar changes of the T waves on August 4th, and about a week after the onset of the attack they became sharply upright in Lead 1 and inverted in Lead 3 in contrast to the opposite directions taken by the T waves previously. Other electrocardiograms taken two months later showed that the T waves eventually became sharply inverted in Lead 1 and markedly upright in Lead 3.

The convalescence was uninterrupted and after a long rest period in bed, during which time no digitalis was given, and in fact, no nitroglycerin was needed, the patient gradually returned to his activities and has continued in very satisfactory health ever since. At present he has no chest pain whatever. The heart shows no murmurs or enlargement. The action is regular, rate is 80. The blood-pressure is 110 systolic, 70 diastolic, and the vital capacity of the lungs is 4075 c c.

Here is an instance of infarct of the heart coming in a comparatively young person. This would immediately make one

suspect an underlying luetic process which was confirmed by frequent Wassermann tests. I think it is highly inadvisable to treat such a patient with intravenous salvarsan. Instead he has been getting mercury and potassium iodid and has done splendidly. It is also interesting that with the low blood-pressure that he now maintains he is free from the discomfort in his chest that previously used to come on effort.

SUMMARY

Attacks of coronary closure are not uncommon, and can easily be recognized by the physician with no other means than what he has constantly at the bedside. They must be clearly differentiated from the more ordinary attacks of angina pectoris, as the prognosis and treatment of the two conditions are quite different. It is important to bear in mind that recovery frequently occurs and that patients are even restored to their active duties. The above 5 cases illustrate most of the important clinical features that occur, and the striking constancy of some of them render it fairly simple to make the diagnosis with a high degree of accuracy. The essential part of therapy is the most complete rest to the mind and body that is possible. Direct cardiac therapy by medication is rarely necessary. Attention to details is of great importance, and when carried out with the utmost care afford a method of therapy which often results in the recovery of the patient.

CONTRIBUTION BY DR JAMES P O'HARE

PETER BENT BRIGHAM HOSPITAL

URINALYSIS

It seems almost absurd to be discussing with graduates in medicine the subject of simple analysis of the urine, and yet I feel very certain that you practitioners can obtain much more information of value from urinalysis than you ordinarily do, provided you pay a little more attention to the details of a proper examination. There is certainly no other laboratory test in the practice of medicine so frequently done and so badly interpreted. You know how the urine examination is most often made—a very rough test for albumin and sugar and nothing else. With these the diagnosis of nephritis or diabetes is made or excluded. The practice of making only very hasty and crude tests for albumin and sugar in the average case and sending the urines of those suspected of renal disorder to commercial laboratories should be condemned. In the first place, the practitioner should know or learn how to make a complete urinalysis, including that of a microscopic sediment. In the second place, many of the commercial laboratories are worthy of but little confidence, and too much is expected of them, even where the work done is excellent. Where the work is done in a scientific manner we should not expect a definite diagnosis remembering always that the urinary findings are only one part of the picture. The same findings may be present in several disorders. If for any reason a man cannot make the examination of the urine himself he should select one of the younger trained men in his district to do these tests for him.

My object today is to discuss the elements that go to make up a proper simple examination of the urine, and to indicate to you some of the information you may expect to obtain from it.

In the first place, let me define what I mean by a "simple examination of the urine" Properly done, it should consist of a test of the reaction of the urine, the determination of its specific gravity, and of the presence or absence of albumin and sugar, and the microscopic examination of the sediment If the patient is thought to have liver or gall-bladder disease, bile should be looked for If sugar is found, tests for acetone and diacetic acid should always be made and the sugar quantitated In a diabetic a twenty-four-hour amount should be analyzed daily until the patient's tolerance is established and it has been demonstrated that he can remain sugar free Then the examination may be repeated every two or three days After the patient's tolerance has been established it is customary for the patient to do his own testing Sometimes in diabetics it is desirable to examine single specimens voided two to four hours after a meal Such specimens may show a small amount of sugar that would be lost in a twenty-four-hour amount

In the nephritic patient the twenty-four-hour amount should be divided into a day twelve-hour and a night twelve-hour quantity It should be emphasized that repeated urinalyses in a suspected case are always desirable Single examinations may fail to disclose abnormal elements or may give us a distorted view of the extent of the trouble As you know, in some parts of the country it is customary for the patient to offer for analysis a specimen of urine voided on arising in the morning While such a specimen may give us some special information about the gravity of the night urine it is, on the whole, about the poorest specimen we can examine What we want to find out is what the urine shows when the kidney is subjected to the strain of the day's activities, physical, dietetic, etc Single specimens voided during the daytime are, therefore, of greater value

Let us discuss some of the practical aspects of these various elements in urinalysis What information do we get from knowing the twenty-four-hour volume of urine? It is, of course, necessary for the determination of the total amount of albumin excreted, if this is desired It is of special value in the diabetic

when insulin is given. Knowing that each unit of insulin is capable of burning 2 grams of glucose, it is easy to calculate how much must be given to take care of a known number of grams of sugar excreted in the urine. From watching the volume of urine excreted one can also tell that a patient with nephritis or cardiac disease is storing fluid or having a diuresis.

With regard to this twenty-four-hour volume of urine there are a few points of practical importance that should be mentioned here. It should always be borne in mind that the volume excreted must be interpreted in relation to the amount of fluid taken in and the amount lost through channels other than the kidneys. Many times have I been told that the urine is falling off in amount, when investigation has shown that the patient has taken by mouth much less fluid or has vomited profusely, or has had diarrhea or profuse perspiration. One should therefore, always think of the volume of urine in relation to the other factors of water metabolism, especially the fluid intake. In hospital cases or those under the care of a nurse it is always desirable to put these cases with a disturbed water balance on a fixed intake of fluid for the day. The volume of urine excreted during the twenty-four hours may be then easier to interpret and have considerably more value.

What information is obtained from dividing the twenty-four-hour volume into a day and night twelve-hour amount? The constant finding of a night twelve-hour volume of urine that is more than one-third of the total twenty-four-hour volume is evidence in favor of chronic nephritis. This, of course, assumes that the individual is not in the habit of taking a large portion of his daily fluid intake during the evening.

The reaction of the urine yields very little information. An alkaline urine, however, may explain the absence of casts which tend to dissolve in such a urine. The chief value of the examination of single fresh specimens is that they are likely to be acid, and casts are, therefore, not so readily missed. In the late stages of a chronic nephritis with hypertension the freshly passed urine may be constantly neutral or alkaline because the patient is unable to excrete an acid urine. A cystitis or pyelitis

caused by the *Bacillus proteus* and certain other bacteria may also show an alkaline urine

The specific gravity of the urine is often misinterpreted. Not infrequently the physician refers to a constantly low specific gravity as evidence of nephritis in a hypertensive patient. This may be true, but it is not necessarily so. One cannot depend on single or even repeated low specific gravities unless one knows that these are not the result of a low diet. In other words, one must know that the patient's kidneys have been subjected to the "test of effort" and that the low gravity indicates their upper limit of excretory ability. We have seen vascular hypertensive patients in whom repeated urine examinations week after week have shown specific gravities of 1.013 or under. Later, when put to the test of a heavy diet, they have been able to concentrate to 1.020, and were proved to have a normal renal function. On the other hand, one must bear in mind that a patient with very severe nephritis may occasionally concentrate to a high level. I have in mind one of my patients who a few days before his death in uremia voided a urine with a specific gravity of 1.019.

Little need be said about the test for sugar in the urine. The Benedict qualitative test is perhaps the simplest and best of the qualitative tests. It is worthy of mention that with this test traces of sugar may occasionally be found in vascular hypertension, subacute and chronic nephritis with edema, renal glycosuria, and other conditions. The explanation for the glycosuria in these cases has not yet been definitely settled. Perhaps they are mild or potential diabetics!

If there is present a sufficient amount of sugar to quantitate, this can be easily done by the quantitative Benedict test. For those who do not wish to bother with this titration method, the old fermentation method, using a saccharometer tube, or even merely noting the difference in specific gravities of the specimen before and after fermentation, is approximately accurate.

Little need be said about the qualitative tests for acetone and diacetic acid. Certainly nothing could be simpler than the ferric chlorid test for diacetic acid. It should be always borne

in mind that the salicylates produce a similar color reaction in this test. The color produced by salicylates is however, but little affected by heating in contrast to the partial clearing following heat when diacetic acid is present.

There is no doubt that the heat and acetic acid test for albumin is a much more delicate test in the urine than is the nitric acid test. Where it is necessary to do more than note the presence or absence of albumin the nitric acid test is a little more satisfactory. With this, when done in a standard way one can designate approximate amounts better than with the heat and acetic acid test. It has been the practice in our clinic to use routinely the nitric acid test, but where no albumin is found in a hypertension patient to try the other more delicate test. Our standard method is first to filter the urine into a wineglass. We then insert carefully at the bottom a pipet containing nitric acid. The latter is allowed to rise slowly under the urine, and the resultant ring of albumin if present is read at the end of one minute. When this ring can just be seen against a dark background it is designated as "s p t" (slightest possible trace). When it can be seen against any background, but cannot be seen from above, it is a "v s t" (very slight trace). When it can just be seen from above it is a "s t" (slight trace). When one cannot see through it from above it is a "t." (trace), and if it is flocculent it is a "l t" (large trace). When the heat and acetic acid test is used we indicate that fact, using the symbol "cl" (cloud) instead of "t" (trace).

It is of course fairly obvious that the degree of albuminuria has very little significance in determining the severity of the disease. A very mild case of subacute nephritis may have a large trace of albumin whereas an almost moribund chronic hypertensive nephritic patient may have little or none. The quantity of albumin is of some value in three conditions. In early acute nephritis the progress of the disease runs for a short time parallel to the amount of albumin. A trace of albumin in a case of longer duration as a rule means one of two things—either subacute subchronic or chronic nephritis with edema or, if the case is hypertensive, an added cardiac passive-congestion

factor This last is not properly appreciated It is usually a fact that a patient with hypertension who has never been showing more than a slight trace of albumin indicates by a trace or large trace that a cardiac passive-congestion factor is at work In cystitis and pyelitis the urine may show only a slightest possible trace of albumin and yet the sediment show much pus

Of all the elements in urinalysis in nephritic patients the examination of the sediment is the most important Certainly the information received is of vastly greater value than that from any other part of the examination It is rather strange, therefore, that it is so often neglected entirely, and deductions made merely from the presence or absence of albuminuria Many times we have seen sediments indicating a considerable amount of kidney damage in urines that showed so little albumin that it might easily be missed It scarcely needs to be mentioned that sediments are of little value in urines that have been standing long, whether they are alkaline or acid Casts may dissolve rather quickly in such specimens Therefore, it is always best to examine sediments from fresh specimens rather than from twenty-four-hour amounts of urine It is worth repeating that single examinations are often very misleading

The examination of the sediment is most important in diagnosis, prognosis, and treatment From its character is determined largely the presence of nephritis and its type, the effect of treatment, and the time for getting the patient out of bed In one particular it is of considerable value in prognosis In nephritic cases the sediment indicates not merely the presence of renal damage but also whether or not there is active tubular breakdown If we assume that Cushny's theory of cast formation is correct, we have at hand a means of indicating the presence or absence of "activity" and its approximate degree Cushny's idea is that all casts are laid down primarily in a hyaline matrix As a result of damage in the glomerular tuft this hyaline material leaks through into the tubules By resorption of fluid in the latter the contents of the upper tubule become acid, and as a consequence the hyaline material becomes coagulated, forming a cast of the tubule where this coagulation takes place This

accounts for the hyaline cast. All others are formed by the embedding in such a hyaline base of red cells, white cells, epithelial cells, and the products of their degeneration, especially tubular degeneration.

With this in mind we can construct a scheme which, while not absolutely satisfactory, is extremely useful in evaluating the casts found in the sediment. The object of this scheme is to indicate to us the degree of active tubular degeneration that is taking place. One can readily understand that a simple glomerular damage without secondary tubular breakdown is indicated by the presence of hyaline casts alone or, at most, hyaline casts and red blood-cells. The latter probably come from rupture of capillaries in the tuft. Where tubule damage takes place this is indicated by the various types of brown granular and cellular casts. The speed with which the tubular destruction takes place is indicated to a large extent by the fineness of the broken-down material. Thus if the tubular cells are desquamated off, the hyaline matrix picks them up almost intact and we have as a result an epithelial cast. If, on the other hand, the degeneration is slight in amount and slow in its production, we are likely to find hyaline casts with just a few almost colorless granules in them. Between these two extremes lie most of the casts found in the urine. The degree of active degeneration can, therefore, be indicated by a series of casts in which cellular casts (epithelial and blood-cell casts) are the most "active." Next in order come the coarse brown granular, then the medium brown granular, and last the fine brown granular cast. The "inactive" casts are the hyaline ones with or without a few colorless granules. In addition to the red blood-cell casts mentioned above in which the cells are embedded in brown granular material there is another type of red blood-cell cast which is merely a colorless hyaline cast with red cells embedded in it. From its construction one can infer no active tubular damage, but merely glomerular leakage and capillary hemorrhage. There are two more types of cast whose origin and significance is somewhat uncertain—fatty casts or hyaline casts with fat in them, and waxy casts. From the close relation between the brown gran-

ules and the fat droplets and from an observation of the changes taking place in certain cases of subacute nephritis we are inclined to feel that these casts indicate some "activity," and should perhaps be placed after the fine and medium brown granular casts. Waxy casts, about which so little is known, indicate, perhaps, a similar amount of "activity" and should be placed with the fatty casts in this scheme.

While blood is one of the commonest findings in the urine of any acute nephritis, it is by no means true that red blood-cells by themselves indicate an active lesion. One has but to consider subacute or chronic hemorrhagic nephritis to realize this. The numerous red blood-cells which, with the exception of a rare hyaline cast, make up the entire sediment, are the result of a mechanical rupture of capillaries in the glomeruli.

White blood-cells are common fairly early in most cases of acute nephritis, but they are much more characteristic in subacute nephritis. In the latter they may dominate the picture so completely that one may feel that he is dealing with a pyelitis or a surgical kidney. In this same type of case the small round epithelial cells so often mistaken for white blood-cells may accompany the latter and be very numerous.

This subject of "activity" of the lesion indicated by the various types of casts found in the urinary sediments is one of great importance, particularly in prognosis. It is well known that the tubular epithelium at least will regenerate if the damage done is not too great and if the irritating element is removed. Function will then improve. Just so long as there is "activity," so long is there a chance for cessation of that activity, and with it a chance for repair. The prognosis should be indeed guarded in all cases of active nephritis. We have in mind 2 cases that demonstrate clearly this principle. One was a man who, shortly after he entered the hospital in 1917, went into uremia with coma and convulsions. His phthalein excretion was 0 per cent, the blood urea nitrogen reached a level of 111 mgm. The blood CO_2 was as low as 16 mm. The blood-pressure was as high as 202/156. Contrary to the fatal prognosis given to his people, and much to our surprise, he began to improve, and since

1917 has been doing ten to twelve hours a day of hard work. He has a chronic nephritis with hypertension, but his phthalein excretion has several times been as high as 50 per cent and his blood urea nitrogen has fallen as low as 23 mgm. His blood-pressure recently was 168/90. Another patient had a very severe acute nephritis in 1919, with a phthalein excretion of a trace, a blood urea nitrogen of 106 mgm and a blood-pressure of 170/100. A fatal prognosis was given to this woman too. And yet she recovered. When we saw her within the past year there was scarcely a trace of her nephritis. The incorrect prognosis given in those 2 cases was due to the lack of appreciation of the fact that we were dealing with an active nephritis. Such cases are, of course, uncommon, but they are by no means very rare.

I have said above that the sediment is one of the most important elements in the analysis of the urine. What may one expect from such an examination? There is much information of diagnostic and prognostic value. Furthermore, it often indicates the effect of your therapy. Omitting calculi, tumors, and the pus infections of the kidneys and urinary tract, in which the microscopic examination of the urine is of the greatest help, and confining ourselves to the nephritides we shall see that the sediment contains elements of great value to us and our patients. From the diagnostic point of view acute nephritis is almost always diagnosed from the sediment. The finding of fatty and waxy casts with an abundance of white blood-cells and small round epithelial cells makes one think immediately of a subacute nephritis. A rare hyaline or red blood-cell cast with a moderate number of red blood-cells in the sediment suggest the diagnosis of hemorrhagic nephritis. Furthermore, in a sediment with many red cells the finding of a few casts, especially if there is among them a red blood-cell cast serves to differentiate such a hemorrhagic nephritis from a silent stone, from tumor in the genito-urinary tract, or from other source of bleeding.

From the prognostic point of view the paragraphs above indicate the importance of an active lesion indicated in the sediment.

Information of therapeutic value may also be obtained. Red blood-cells with or without cellular or brown granular casts calls for a continuation of physical rest until these elements have disappeared completely or until it is obvious that no further gain can be expected from more rest. The sediment of every patient with active nephritis should be closely watched after he is allowed to get out of bed. An increase in the blood-cells or granular casts is an indication to put the patient back in bed for more prolonged rest.

From the facts given above it can very readily be seen that the ordinary simple analysis of the urine yields information of the greatest value for diagnosis, prognosis, and treatment. It is up to the physician to avail himself of this information which is so close at hand.

CLINIC OF DR C W. McCLURE
EVANS MEMORIAL HOSPITAL, OUT-PATIENT SERVICE

DIAGNOSIS OF PEPTIC ULCER AND CHOLECYSTITIS

THE rather brief exposure to this clinic, to which you students are subjected, must have impressed you with the frequency of the diagnosis of two conditions, *i e*, ulcer of the stomach or duodenum (peptic ulcer) and chronic disease of the gall-bladder (cholecystitis). It may have appeared to you that the diagnosis of these conditions has become an unwarranted practice in this clinic. It may have seemed to you that our clinical and experimental studies on these conditions have warped our judgment. Of course, the special abdominal surgical service maintained in the hospital in connection with Dr J Emmons Briggs allows us to check up at the operating table on a fair percentage of our diagnoses. But there still remains a goodly number of patients who do not come to laparotomy. Many of these have had other diagnoses made in different clinics, and you may question the correctness of our diagnosis of ulcer or gall-bladder disease. Whether our diagnoses are accurate rests upon two factors: (1) on the correctness of our conception of these two clinical entities, and (2) on the completeness and accuracy with which the symptomatology of each case is obtained. We wish to discuss these factors along with certain illustrative cases this morning.

Of first and of incomprehensively great importance is the history given by the patient. For practical purposes we are in the habit of dividing the subjective symptomatology into the less distressing *dyspeptic* and the more disturbing *serious* trains of symptoms. The *dyspeptic* train consists of nausea, vomiting, heart-burn, water-brash, regurgitation, belching, anorexia, epigastric distress, distress in other abdominal regions, constipation, and diarrhea. The *serious* train of symptoms comprises jaun-

dice, pain, hemorrhage, obstipation, sudden constipation, more slowly developing and unexplained constipation, and the presence to a marked degree of one or more of the symptoms grouped under the *dyspeptic* train

Having obtained a list of subjective symptoms, it is necessary to establish which ones are most marked in the degree of their severity, their relation to the ingestion of food together with the times of day or night at which they occur, the total period in days, months or years of their duration, and whether they occur periodically or sporadically. In other words, the history should establish the character, severity, duration, and chronology of the subjective symptoms

The occurrence of certain important symptoms may be established either subjectively or objectively, or by both means, such as weakness, loss of weight, hemorrhage, jaundice, fever, chills, etc

The physical examination establishes the presence of possible anemia, cachexia, jaundice, tumor, abdominal tenderness or muscle spasm, abdominal fluid, herniæ, etc. Usually in this clinic the most important data furnished by the physical examination are those findings which aid in ruling out extra-abdominal causes for the presenting abdominal symptoms, which latter may occur as the result of cerebrospinal disease, lead-poisoning, pulmonary and cardiac disorders, and various other pathologic entities. In fact, when considering the diagnosis of the cause for gastro-intestinal symptoms always remember that such symptoms may accompany almost any ailment to which the human flesh is heir

The x-ray examination of the gastro-intestinal system is an integral part of every complete physical examination of the "abdominal" patient. This examination should comprise plates of the gall-bladder region and of the kidneys for possible calculi. Fluoroscopic examination of the stomach and intestines, and a barium enema when indicated, complete the x-ray studies. The superior advantages of fluoroscopy of the stomach and intestines over plates will be discussed in relation to certain cases later on

Laboratory examinations frequently furnish important data. It does not take more than ten minutes to establish the presence or absence of anemia, of leukocytosis, eosinophilia, or blood-parasites, while only occasionally are the more complicated estimations of the concentration of blood urea or sugar indicated. The stools can be quickly examined for diarrhea, blood, pus, excessive amounts of mucus, gross evidences of undigested food, parasites, or occult blood. Inspection of vomitus for old food residues, blood, or "fecal vomiting" is always important. The presence or absence of free hydrochloric acid in the vomitus or gastric contents removed by tube is sometimes helpful in the differential diagnosis between a benign and a malignant condition. These examinations can be very readily made. On the other hand at the present time, examinations of duodenal contents are time consuming as well as complicated. However in selected cases the information so gained justifies carrying them out.

This morning's clinic consists largely of patients who are no longer under active treatment, but who report at intervals to allow their progress to be ascertained. This will afford material illustrating some of the phases of the diagnosis of peptic ulcer and gall-bladder disease. The discussion will be confined to the essential findings in each case. The complete record may be read by any of you who so desires.

The first patient is a man of about forty-five years and presents a typical case of ulcer. He is a mechanic by trade. The past medical history of this patient is essentially negative except for the gastro-intestinal tract. He entered this clinic a year ago, complaining of epigastric pain. At that time he had lost about 10 pounds in weight over a period of six weeks.

The onset of the gastric symptoms occurred six years prior to admission to this clinic. It was characterized by distress and sharp pain in the epigastrium, occurring regularly a hour after meals. The pain radiated to the dorsolumbar region. It was more or less relieved by soda and by a glass of milk. Not infrequently pain awakened the patient between the morning hours of 1 to 3. The present attack was of about six weeks'.

duration Since the onset, six years ago, attacks similar to the present one had occurred every three to six months, and had persisted from two to six weeks There had been no jaundice, no vomiting, and no bloody or tarry stools At the time this history was taken the physical examination was essentially negative The fasting gastric contents contained no food residue Free HCl was 50 The benzidin test for occult blood was negative The usual examinations of the blood, urine, and stools were negative Fluoroscopic examination showed a stomach of normal contour and position It was freely movable At the end of six hours very little of the barium had left the stomach Peristalsis of the stomach was vigorous, showing three deep waves The pyloric sphincter showed only a slight degree of pylorospasm and the cap filled improperly, *z c*, it was irregular in outline

At laparotomy there was found a duodenal ulcer with considerable stricture of the pyloric orifice

Analyzing this patient's history, the distinguishing diagnostic feature was the time relation between the taking of food and onset of epigastric pain A note made later on in the record shows that the pain was of variable severity, varying from mild to severe But it was always true pain, and it always bore a definite time relation to the ingestion of food Another characteristic feature is the fact that the symptoms occurred periodically, *z c*, there were periods of freedom from symptoms, then symptoms developed and persisted a considerable time Other less important, but characteristic symptoms, were the relief afforded by food or soda, and the occurrence of pain during the early morning hours Backache was also present Sometimes pain in the dorsolumbar region is the most distressing symptom during the relapse of a peptic ulcer, and because of this I have several patients who were studied first by orthopedic and by genito-urinary men for spinal arthritis and for renal stone

One feature of the case under discussion deserves special mention, and that pertains to the fluoroscopic findings, which showed a marked degree of food retention in the stomach Now,

a plate would have demonstrated the same phenomenon. But the fluoroscope allowed it to be seen that the pyloric sphincter never showed more than a slight degree of spasm. This absence of pylorospasm was strong evidence that the food retention was the result of an organic stricture of the pylorus, and this was found at laparotomy. You may ask why the patient did not vomit. Well, his record shows that his diet was of semisolid nature, as a rule, and had been entirely of liquid nature during the present relapse of six weeks. Furthermore, he is a scanty eater at all times.

In the relapse just described the patient was placed on a liquid and semisolid diet of entirely bland nature. But, as was to be expected, no relief was experienced. I say "as was to be expected," because of the degree of obstruction. Since he did not respond to medical treatment, laparotomy was performed.

The record of this patient, then, gives the findings usually presented by a typical case of peptic ulcer except for the absence of hemorrhage. Such typical symptoms may be summarized as follows:

The patient presents himself complaining of epigastric pain occurring at a fairly definite time after meals, and relieved by soda or food, or less often by vomiting which is usually induced. Occasionally the pain radiates, and most often to the dorso-lumbar region. Frequently night pain is a distressing symptom. Although hematemesis and tarry stools occur in a considerable percentage of cases, the occurrence of these phenomena in relation to the duration of the disease and the number of exacerbations is relatively infrequent. Rather rarely vomiting is a prominent symptom. Belching, regurgitation, and other dyspeptic symptoms occur frequently, but, as a rule, they are not particularly distressing to the patient. Constipation is the rule, although the bowels are occasionally regular. The radiographic findings show either some type of deformity in the stomach or duodenum, or some type of disturbed peristalsis or muscular action often associated with spasm of the pylorus. The gastric contents contain free HCl. The stools and blood show nothing unusual unless hemorrhage has occurred.

The history as given by the patient under discussion is sufficient to make the diagnosis of peptic ulcer with a considerable degree of accuracy. His history together with the fluoroscopic and other findings, is almost diagnostic of ulcer. However, such findings may be simulated by cancer. We have just witnessed an operation which illustrates this, a laparotomy on a patient from this clinic.

This patient was a man of fifty-five. He considered himself well, up to May of this year. At that time mild diarrhea of unexplained cause developed. It consisted of two or three semisolid or watery stools a day. It was unaccompanied with any other abdominal symptoms. In July there developed persistent epigastric distress, which was but slightly affected by food. In October moderately severe epigastric pain began. This pain developed regularly two hours after meals, and it was relieved by alkalies, food, or induced vomiting. There was no involuntary vomiting and no nausea. The appetite remained fairly good. From May to December, the patient fell off in weight from 172 down to 138 pounds. Most of this loss occurred in October and November, and was ascribed to limited intake of food. In the last week of November the patient became constipated and opened the bowels with an enema. The resulting stool was of a tarry nature (showing that a hemorrhage had occurred high up in the gastro-intestinal tract). At this time physical examination showed nothing other than evidences of loss in weight. The blood showed hemoglobin to be 80 per cent, 4,500,000 red cells and 8000 white cells. The blood-smear was not unusual. The Wassermann was negative. Stools were semisolid, but not otherwise abnormal. The urine was negative. x-Ray studies showed twenty-four-hour retention of the barium meal. The character of the plate of the stomach was like that of a benign pyloric obstruction. Since it was absolutely necessary to relieve the obstruction by surgical means, the patient's wish not to take the stomach-tube was granted.

The diagnosis of peptic ulcer was based on the character of the pain and on the x-ray findings, but at laparotomy cancer was found. However, there was one feature of the history

which the diagnosis of peptic ulcer did not explain, *i. e.* the diarrhea. Constipation or, more rarely, regularity of the bowels is the rule in the presence of peptic ulcer.

Three patients are present this morning whose condition was diagnosed as a neurosis in various clinics, and with considerable justification. But, although each of these patients was and still is "neurotic," each had some organic lesion, *i. e.*, peptic ulcer. The first patient is a man of forty, and a shoemaker by trade. For six years he had periodic attacks of pain developing one to two hours after food, the pain was located in the left lower abdominal quadrant. Such attacks persisted several weeks and then remitted for several months. The pain was relieved by either soda or food. It was usually of mild character, but occasionally was of severe, colicky nature. The bowels were constipated. There was no nausea or vomiting, and no hematemesis or melena. The appetite was poor, and there was belching, some water-brash, and heartburn. The remainder of the history was non-essential and the clinical laboratory examinations of blood, urine, and stools were negative, as was also the blood Wassermann. Gastric analysis showed a usual amount of free HCl. α -Ray studies, with plates of the stomach and duodenum, were reported as negative, but on subsequent fluoroscopic examination gastric peristalsis was found to vary in activity. At times it was hyperactive and at other times sluggish or quiescent. This type of peristalsis results from some lesion which irritates the stomach. By turning the patient in the proper position the first portion of the duodenum was seen to be very much distorted. No abnormalities were demonstrated in the remainder of the small intestines or in the colon after a barium enema. The findings in this patient caused the diagnosis of duodenal ulcer to be made, and such a lesion was found on laparotomy. It is fair to other physicians to say that this patient was under great emotional strain for a long period of time due to protracted illness of his wife. This gave a basis for the development of a neurosis which existed. But an organic lesion also existed. Furthermore, α -ray plates had failed to demonstrate a lesion in the gastro-intestinal tract.

However, the patient had real abdominal pain, with definite time relation to meals, although the pain was in the left lower quadrant. There was, also, the characteristic fluoroscopic findings of an ulcer. The abnormal location of the pain described by this patient has been observed in one other patient with duodenal ulcer of this clinic. Again, the record of the patient demonstrates the advantage of fluoroscopy in gastro-intestinal studies, for only by it was the ulcer demonstrated.

Mrs. G. is another patient who had been diagnosed as neurotic over a period of years. As a matter of fact, she is neurotic, but she has apparently an ulcer of the duodenum also. This patient is forty-two years old. She is the mother of several children, and she has always worked too hard, besides having many worries. Since the age of puberty vomiting has been associated with menstrual periods. For a "number" of years the patient has had attacks of headache accompanied with vomiting and severe dorsolumbar pains. During these attacks the appetite is good, but food causes nausea. Such attacks last a period varying from a few hours to a few days, and recur at frequent intervals. Two years ago very typically bloody stools were passed on two occasions. Most of the time the patient feels "heavy and dull." She has lost weight. The remainder of the history is non-essential, and the physical examination shows nothing of diagnostic value. The usual clinical examinations of blood, urine, and stools are negative. The blood Wassermann is negative. Gastric contents show free HCl, functional tests of the pancreas and liver, as determined in this clinic, are negative. X-ray studies were first reported negative. It seems to be the rule for radiographers to disregard fluoroscopic findings not verified by plates of the stomach and intestines. At any rate, the x-ray report came back as negative. But, as a matter of fact, fluoroscopic examination of this patient's duodenum shows a well-marked and characteristic deformity in the duodenum. But, in order to see it, the patient must be turned in a lateral position and the stomach pushed to the side by pressure on the abdomen with the hand. Pressure thus exerted must be made in such manner as

not to distort the region under examination, and the proper technic can be acquired only by experience

The essential findings in this patient are, then, severe symptoms with pain have been present for "a number" of years. Melena has occurred. Fluoroscopy shows a lesion corresponding to that of a duodenal ulcer. The liver function, so often abnormal in the presence of chronic cholecystitis, is normal. The findings, noting especially the melena, are quite characteristic of duodenal ulcer. Remember that the pain was in the dorsolumbar region, i. e., in the back. Many cases have failed to be properly diagnosed because the pain in the back is so prominent that the physician does not believe an ulcer can cause it, but some cases of duodenal ulcer never have pain in any other region than the back.

These 3 patients forcibly call our attention to a warning of vast importance in the every-day practice of medicine, i. e., never call any patient simply neurotic who complains of true abdominal pain, or of severe dorsolumbar pain or who gives a history of having either passed bloody stools or of having vomited blood. Furthermore, make sure that your radiographer does a careful fluoroscopic examination of the stomach and duodenum in the course of his x-ray studies, and that he does not neglect to report apparent abnormalities found by that examination.

The more experience each of you students obtain, after you have entered the practice of medicine, the less often will you make the diagnosis of a neurosis. This will happen because experience will teach you to see evidence of lesions of organic character which you were unable to recognize or even suspicion with a lesser degree of experience.

Here is a patient whom I thought had a cancer. He entered this clinic emaciated and deeply jaundiced, but before operation the diagnosis of cancer was changed to that of benign lesion for reasons that will be discussed later. The essentials of this patient's history are as follows. The patient is a man of forty-seven years. He is a mechanic by trade. The patient's gall-bladder was excised because of chronic cholecystitis accompanied

by gall-stones in 1922. At the same operation an ulcer was found on the lesser curvature of the stomach, near the pylorus, and was excised. The operative recovery was uneventful. Since that time the patient had considered himself cured of all his abdominal ailments for a period of two years. He then began to lose his appetite and to be bothered with persistent nausea and constipation. After a few days of these symptoms vomiting immediately after meals developed. After a period of two weeks the onset of icterus occurred. Two weeks later he consulted me in the clinic. At that time he was deeply jaundiced, had lost much weight, and gave a history of passing tarry stools every few days. There was, and had been, no abdominal pain. On physical examination the patient showed emaciation and deep icterus. A ventral hernia existed at the site of the former laparotomy. Examination of the stools showed them to be dark with blood. The duodenal contents contained a high concentration of bile. The blood showed a considerable degree of secondary anemia, *i. e.*, hemoglobin 50 per cent, red cells 3,100,000 and 13,000 leukocytes. The blood Wassermann was positive. *x*-Ray examination showed distortion of both the pyloric end of the stomach and of the duodenum.

The patient's history and progress were like that frequently encountered in cases of jaundice secondary to cancer of the head of the pancreas, but such a condition would not account for the bloody stools. Furthermore, when cancer of the head of the pancreas becomes extensive enough to involve the common duct sufficiently to cause deep jaundice, one will not get a high degree of concentration of bile in duodenal contents removed by the tube. These findings, together with the previous history of gall-stones and ulcer, led us to finally diagnose the condition as duodenal ulcer accompanied by some type of benign obstructive jaundice. *x*-Ray findings agreed with this conception of the case, but they were of chief aid in excluding cancer of the stomach, adhesions due to the previous operation could have given rise to the abnormalities of the stomach and duodenum shown by the *x*-ray.

Thus, you have seen this morning typical cases of peptic

ulcer, a few atypical cases, and a case of gastric carcinoma in which the preoperative diagnosis was peptic ulcer. In addition to the atypical types of ulcer shown, there occur other types. The commonest of these are as follows: cases in which the pain resembles that of a gall-stone colic, cases in which there is constant epigastric pain, which may be but little modified by food, cases with persistent vomiting and with little or no pain. The diagnosis in these cases is usually aided very greatly by x-ray studies and by studies of the pancreatic and biliary fractions of duodenal contents. In such cases it is important to ascertain the presence or absence of free HCl in gastric contents. Free HCl is almost invariably present when ulcer exists, its absence speaks in favor of cancer or chronic cholecystitis.

Now a word as to the treatment of peptic ulcer. In my experience medical treatment is fully as safe and just as satisfactory as surgical. Of course, one must not treat medically a patient with evident surgical complications, such as perforation, a high degree of pyloric obstruction, perigastric abscess, some types of hour-glass stomach, and persistent hemorrhage. The real objection to medical treatment is the difficulty of keeping the patient at it after he considers himself well. The price of "cure" in peptic ulcer is "eternal vigilance", and if you expect to keep the patient well you must keep him under both observation and treatment the rest of his life. These patients often refuse to undergo, and they frequently relapse as a result of their own negligence.

CLINIC OF DR EDWARD S EMERY, JR.

PETER BENT BRIGHAM HOSPITAL

DISORDERED FUNCTION OF THE COLON¹

THE first case to be shown (A M O Med No 23,643) is that of an Irish woman, forty years of age, who entered the hospital May 8, 1924, complaining of diarrhea, cramps, and loss of weight. The patient had been well until two years before, when for a period of about a year she had weekly attacks of diarrhea accompanied with abdominal soreness and cramps, lasting two to three days at a time. The stools were always greenish and slimy. From then until two months ago she has had no diarrhea, but the cramps have continued at intervals. During the past eight months she has vomited colorless mucoid material. Two months ago she was put on a bland diet, with rest in bed, and her diarrhea ceased, although her cramps continued.

The abdominal distress consists most frequently of general abdominal cramps, usually more severe below the umbilicus. In addition, she frequently has fulness in the epigastrium and a sensation of being distended with gas. The symptoms may come on at any time throughout the day, and are made worse by eating. She has a great deal of rumbling and belching, which give slight amelioration of the symptoms. A bowel movement may make all the symptoms better or worse, frequently bringing them on. Soda gives little or no relief. The patient has been taking castor oil every other day for the past year, as it gives temporary relief.

Physical examination was essentially negative, except for the abdomen, which revealed generalized tenderness, more on

¹ From the Medical Clinic of the Peter Bent Brigham Hospital

the right side There was also considerable spasm of the abdominal muscles, particularly the right rectus

Laboratory examinations showed the urine to be acid, specific gravity 1019 to 1032, albumin 0 to the slightest possible trace, sugar 0, sediment negative Blood, hemoglobin, 105 per cent (Sahli), red blood-cells, 4,750,000, white blood-cells, 7000, differential count and smear negative

Gastric analysis showed a total absence of free HCl, but the microscopic examination was negative All stool examinations showed them to be mushy or watery and containing much mucus

a-Ray examination of the stomach and intestine was negative A barium enema revealed a smooth colon, free of haustration, typical of a so-called chronic colitis

The next case (J B L Med No 24,846) is a man fifty years of age, whom I saw first at my office three months ago At that time he gave the following history He had always been well until three years previously, when he began to be troubled with "indigestion" This consisted of a sensation of fulness or weight in the epigastrium, coming on around 10 A M or 4 to 5 P M On occasions it would return around 10 P M Soda gave relief, but whether before or after belching he is not sure Eating usually gave relief, but not invariably He had vomited on two occasions, with some relief All of the foregoing suggested ulcer, but the distress might come on before breakfast (which if due to ulcer required a twelve-hour retention), and at times he believed it would be made worse with eating Belching also gave some relief In addition to the above, he was troubled a great deal with the sensation of gas and distention and had considerable abdominal rumbling and gurgling At times he would have cramp-like pains below the umbilicus He had not noticed the effect of a bowel movement or the passage of flatus His bowels moved once daily, but he had never noticed the character of his stools He gave a history of drinking considerably, and on occasions would take enough to become intoxicated He believed his drinking had much to do with his symptoms An a-ray of his stomach showed no pathology At this time he was unable to enter the hospital, so he was given a diet, and

because of the suggestion of ulcer symptoms he was advised to watch his distress closely and to return again in a week. However, he was not heard from again until he entered the hospital November 13, 1924.

At this time he had been intoxicated for several days and was suffering from severe abdominal cramps. At this entry he was able to say definitely that his distress would occur before breakfast. He had also noticed that bowel movements and passing flatus gave temporary relief. His L. M. D., moreover, stated that when he was not drinking he would be entirely free of symptoms.

Physical examination was essentially negative except for a palpable liver edge 4 cm. below the costal margin.

Blood hemoglobin, 85 per cent, red blood count, 4,900,000, white blood-count, 10,400, smear negative, Wassermann test negative.

Gastric analysis showed free HCl 105, T. A. 135. Sediment, occasional white blood-cell. Benzidin negative.

A barium enema revealed an extremely irritable colon, and it was impossible to get the barium beyond the rectum, as the patient was unable to retain it owing to the marked contractions.

Stools were softer than normal, and occurred twice a day on a non-residue diet. Visible mucus was present in all. Microscopic and benzidin examinations were negative.

The third case (J. L., Med. No. 24,653) is a man thirty-nine years of age whose complaint is abdominal pain, eructation of gas and loss of energy. Family history and past history are unessential.

The present illness reveals the fact that the patient has been troubled with abdominal distress for the past twenty years. Three years ago he had severe cramp-like pain around the umbilicus lasting five to six days. A diagnosis of chronic appendicitis and gall-bladder disease resulted in an operation, but both organs were found to be normal. The cramps persisted and the patient began to complain of frequent eructations of gas. He started to lose weight, feel tired, and two years ago he went to California, where he was put on a raw fruit and vege-

table diet, under which his symptoms became worse and have continued till the present time. He has vomited at times when his symptoms have been most severe.

The distress consists most frequently of cramp-like pain situated for the most part in the lower half of the abdomen, but not infrequently centered around the umbilicus. In addition, he is bothered with "much gas." This is manifested by distention in the upper half of the abdomen and belching. The distention may be so severe as to cause difficulty in the patient's breathing.

The discomfort may occur at any time in the twenty-four hours, but the distention is very likely to come on within fifteen to twenty minutes after eating. He has noticed that although eating usually makes it worse, occasionally it gives some relief. Partial relief is obtained with belching, and with soda after belching has occurred. Bowel movements always influence the distress, at times increasing it, at other times relieving it. He has noticed that certain foods always make him worse, and as a result he is afraid to eat food-stuffs such as cabbage, pears, and apples.

His bowels move once or twice daily, but he has not noticed their consistency.

Physical examination shows some pyorrhea. The abdomen is soft and shows a scar in the R L Q. Cecum, descending colon, and sigmoid are easily palpable.

Gastric analysis gave free HCl 40, T A 54. Microscopic examination negative, benzidin negative.

Blood showed hemoglobin, 85 per cent, red blood-cells, 5,110,000, white blood-cells, 7100, smear negative, blood Wassermann negative, urine entirely negative.

A diagnostic enema produced the same kind of distress of which he complained after the injection of 1 pint, 3 pints caused severe pain and he was unable to retain it. x-Rays revealed no pathology.

The patient's stools showed an increased amount of mucus, and the only one obtained on an ordinary diet was softer than normal.

Benzidin was negative at all times

Comparison of the Three Cases—We have shown you 3 cases. The first one is commonly diagnosed mucous colitis, the second one acute or chronic gastritis, and the third one is given one of several different diagnoses, such as gastric neurosis, chronic indigestion, intestinal indigestion, or even neurasthenia, suggesting that these cases represent disorders respectively of the colon, stomach, and small intestine. Let us now compare the 3 cases.

All have been troubled with a sensation of distention. With this sensation goes a fulness in the epigastrium, which is interpreted by the patient as due to gas. All of them belch a great deal, with some relief. All have had rumbling and gurgling, with resulting temporary relief. Soda gives relief only after belching. Bowel movements and passage of flatus would definitely modify the patients' symptoms either for better or for worse. All 3 patients have been occasionally bothered with nausea and vomiting.

On examining the stools we find that invariably they have been softer than normal and that the patients were accustomed to have two or more stools during the day, despite the fact that they were having food containing much less residue than a normal person would eat. Mucus was present in the stools of all cases.

Barium enemas gave the same findings in each case, although varying in degree. There was a tendency for the colon to contract spasmodically, so that the barium failed to flow in smoothly and easily, and filling the colon invariably caused distress similar in character to the symptoms which caused the patient to seek medical advice.

Now when we study the stomach we obtain negative x-ray findings in all 3. In one there is an achylia gastrica, in the second case there was a so-called hyperacidity with a free HCl of 108, whereas, in the third case the findings are essentially normal, with a free HCl of 40.

In these 3 cases, therefore, the findings point to a disturbance of the colon, and we have no evidence to incriminate the stomach as a cause of the patients' symptoms. I have shown you these 3 cases because the first is one that is generally recognized and

diagnosed as a disturbance of the colon. The second case, with his attacks of acute cramp-like pain, will be recognized as intestinal in origin, but after the acute symptoms have subsided the general tendency would be to look toward the stomach as the cause of his trouble, and finally, the third patient is the type which passes under the various diagnoses spoken of previously.

It is this latter type of case which I wish to emphasize as being due to a disordered functioning of the colon. And I have attempted to point out the similarity between the symptoms and findings between the case which is commonly recognized as having a chronically disturbed colon, and the last case, which is usually not considered at all from the standpoint of the colon.

The Functionally Disturbed Colon from a Clinical Standpoint—For many years there was a tendency to lay all the symptoms of so-called indigestion to trouble with the stomach. This was a result largely of the work of Kussmaul who, in 1867, wrote on the value of the stomach-tube in dilatation of the stomach. The use of the tube gave a means of studying the gastric secretion, and as it was about the only means known of studying the gastro-intestinal tract objectively, it was a logical result that abdominal symptoms should be explained on the basis of a hyperacidity or hypo-acidity. With Van den Velden's discovery in 1879 that the HCl was decreased in carcinoma of the stomach, a great impetus was given to this means of study, and tended to increase interest in gastric aspirations as a diagnostic procedure. The tendency to lay all distress of the gastro-intestinal tract upon the stomach continued, chiefly because of the lack of sufficient knowledge, and Riegel, as late as 1903, writing on Diseases of the Stomach in Nothnagel's Encyclopedia Of Practical Medicine, Amer. Ed., page 112, stated that "Cases of hyperacidity are quite frequently seen in which no high values of hydrochloric acid are found on quantitative analysis," and again, "Cases of abnormally high hydrochloric acid excretion are seen that show no symptoms of hyperacidity." In other words, he recognized the incompatibilities, but was unable to explain the symptoms on any other basis.

Within recent years, largely through the efforts of a few

clinicians, we have begun to recognize the colon as the source of various digestive complaints. The late Dr. Bertram W. Sippy had made a very close study and classification of these symptoms, and it is to him that I am indebted for much that I know about these cases.

Symptoms are diverse. They may occur at any place in the abdomen, and may vary from the mildest type of distress, such as a slight fulness or heaviness or weight, to the most severe cramp, as typified by the schoolboy green apple colic. Patients usually complain of distention and frequently loosen their clothes to obtain relief. Most patients complain of an excess of gas with gaseous eructations, and become the chronic belchers who are so familiar to us all.

As to the time of occurrence, the symptoms very frequently manifest themselves before breakfast, thus differing from peptic ulcer, which gives discomfort before breakfast only when there is a twelve-hour retention. Another difference from ulcer symptoms is that the distress is quite haphazard in its appearance. Although tending to come on within a few minutes after eating, the symptoms of gas belching, etc., may be troublesome at all times of the day or night. The distresses may be intermittent in character, differing from the remittent pain of ulcer.

The symptoms are brought on or aggravated by many factors.

Certain food-stuffs, such as cabbage, apples, pears, are a frequent cause of the symptoms. Patients have learned by experience that the eating of such kinds of foods will be followed by the sensation of gas, distention, rumbling and gurgling, or more severe types of distress. Oftentimes our patients have ceased to eat certain foods, as they have found these things disagree. Cold substances are often the cause of immediate distress. Thus ice-cream will lead to discomforts of one kind or another, but if warmed in the mouth before swallowing it will be tolerated perfectly well. Severe shaking as brought about by riding over rough roads may cause discomfort. Chilling the surface of the body, as in swimming, is another disturbing factor.

Those things which mechanically stimulate the colon may

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Those things which mechanically stimulate the colon may

cause the distress, such as a bowel movement, the giving of an enema, or massage of the colon. Likewise these procedures may give relief when distress is present. Cathartics should likewise be classed as a cause of this distress even though they may seem to give temporary relief.

Relief from the symptoms may be produced by bowel movements, enemas, and massage. Belching gives temporary and partial relief, and many of these patients are chronic belchers, swallowing and eructating in the hope that the next belch will sufficiently relieve them. It is for this reason that soda is taken by so many, as the gas resulting from the mixture of HCl and carbonate distends the stomach, and the resulting belch mechanically relieves the distress. Therefore, it is always well to ask a patient whether their relief from soda occurs before or after belching, as in the former case it will be an ulcer distress, whereas in the latter it may be colonic.

Heat is usually very efficacious, and warmth applied to the abdomen in the form of a hot-water bottle or an electric pad is a useful means of temporarily alleviating discomfort.

Physical examination may reveal considerable local or even generalized spasm, although, of course, in the mild cases the abdomen may appear quite soft. There is usually tenderness over the colon at some area, or the entire colon may be sore to pressure. Normally one can feel only the cecum, and the palpation of other portions of the bowel is abnormal. In these cases it is not uncommon to feel the descending colon as a cord-like structure. It should be remembered also that normally one should obtain a splashing sound in the abdomen only over the cecum and ascending colon, and over the stomach only after a meal, but with this type of case it not infrequently happens that we can elicit splashing sounds over the transverse or descending colons.

Another sign which is occasionally made out in rather severe cases is obtained by stroking the abdomen. As the instrument passes midway through a line from the anterior superior spine to the umbilicus, there is a marked skin reflex.

In the study of these cases the stools are of great value to us

If we consider the physiology of the colon for a moment, it will be remembered that the intestinal contents enter the cecum in a liquid or semifluid state. As the fecal material is pushed along, fluid is absorbed, so that by the time it reaches the splenic flexure it is of the correct consistency to be evacuated. With the occurrence of a proper stimulus the descending colon empties its contents into the rectum, and the resulting distention gives the desire to defecate. With the granting of this desire we obtain a normal stool which is one that is firm enough to hold its shape, but at the same time is soft enough to be molded, so that it can traverse the rectum and anus without difficulty.

From this it is clear that any stool harder than normal means that too much liquid has been absorbed, which, in turn, means that it has resided in the colon too long, and that the colon has not pushed its contents through rapidly enough. Conversely, a stool softer than normal means too little fluid has been absorbed and that the colon has pushed its material through too rapidly. In this way the stools give us a guide as to the state of activity of the large intestine. If now we find that under normal conditions a patient is passing stools softer than normal, we are justified in saying that the patient's colon is unduly irritated. And this is a common finding in the type of case we are discussing. If you recall, all 3 of the patients shown today have been having stools softer than normal. There should not be a positive test for blood, as this type of case does not have ulcers or erosions to cause bleeding.

A certain number of acutely irritated colons run an increased white blood-count, but this is not the rule, and with a leukocytosis we must be very guarded in putting a patient in this classification. Whether this condition can produce an increase in temperature I am not yet prepared to say. I should be extremely wary of any case with a fever and leukocytosis, even though every thing else pointed to this type of condition.

Finally, we can give a barium enema. The barium tends to flow intermittently, being held up by contractions, which finally relax, allowing the barium to run ahead 2 to 6 inches before being stopped again. The colon usually shows an in-

creased activity, and may contract so violently as to make it impossible for the patient to hold the injected fluid. Meanwhile, we should question the patient as to the production of any discomfort, as a perfectly normal colon can retain from 2 to 3 quarts without difficulty.

To sum up, then, there is a type of case such as this third patient I have shown, which is well known to all medical men and in whom we find evidences of an irritated colon. By comparing him with the first case, which is commonly recognized as a disturbance in the colon, we see that the symptoms of these 2 vary only in degree. If you follow enough of these cases closely you will find that wherever there is found these symptoms you will be able to demonstrate the signs of an irritated colon or, using Dr Sippy's terminology, an irritable colon. Reasoning backward, it seems fair to assume that the symptoms which we have discussed are in some way produced by the colon, and that many of the symptoms which formerly have been attributed to the stomach are in fact not gastric at all.

Discussion of the Pathology—The more I study this kind of case, the more in doubt I become as to just what is taking place. Nothing has been demonstrated pathologically to give us any help. Grossly and microscopically the colons appear normal, although Soper believes that the blood-vessels are not quite so evident at proctoscopy.

All that we can say is that in these cases the colon contracts with a smaller stimulus than in the normal case. We have to do with a nerve and muscle apparatus about the physiology of which we know little.

At present I like to think of this mechanism as having a threshold value at which it will respond to a given stimulus. If we lower the threshold a smaller stimulus will be required to touch it off, and if we can raise it, a larger stimulus will be required, but this, of course, does not explain the cause of the raising or lowering of the threshold.

The colon consists of a tube made up of smooth muscle and a complex system of nerves. The nerves are for the most part of the autonomic system and go to make up Auerbach's and the myen-

teric plexuses In addition, the central nervous system plays some rôle, as is evidenced by the well-known fact that mental excitement may produce a diarrhea Now this colonic mechanism always has a certain stimulus acting upon it in the form of the intestinal contents Under normal conditions the stimulus to activity is such that the mechanism works as it should Under these conditions we know by experience we can throw the system out of order in one of two ways Returning to the idea of a threshold value, we can leave this unchanged and increase the stimulus sufficiently to break through This may be done by the excessive use of cathartics, excessive use of alcohol, or the continued use of unduly irritating food A single application of the increased stimulus by these means results in temporary derangement, with diarrhea and cramps, which subside as the stimulus subsides If continued over a long period of time a chronic condition is set up which takes a longer time to recover from

On the other hand, the stimulus may be kept constant and the threshold lowered This would appear to be the situation in the cases before mentioned, when, through anxiety or mental excitement, an individual is seized with diarrhea and cramps And this seems to be the situation in the cases with an unstable nervous system This is what we have in the so-called neurasthenic or neurotic individual These cases have a low threshold value normally A stimulus that can be tolerated in the average case will be too much for the nervous individual

The treatment of these cases, therefore, is to allow only such stimuli to reach the colon as shall be in keeping with its threshold value In those cases where the trouble is due to excessive stimuli with normal threshold values the solution is simple By cutting out whatever irritating cause has been operating, we can be assured that the trouble will quickly mend Thus in the second case that we have shown, if we can get him to stop the excessive use of alcohol, his symptoms will rapidly disappear The last case will be more difficult There the ideal procedure would be to build up his threshold value But this leads to the whole question of the underlying condition of

the neurasthenic To give him relief from his symptoms we must cut down the stimuli reaching his colon until he is receiving only an amount sufficient to have his colon respond in a normal manner as evidenced by freedom from distress and the obtaining of a normal type of stool In the second case the problem is simple, for we are simply causing the patient to live an average life The third case is harder because we must limit his type of life below that of the average individual Of course, between these two extremes we have all combinations

In short, however, the ultimate aim of treatment is to give the patient's colon an opportunity to quiet down And this is accomplished by eliminating all irritating agencies, such as cathartics and enemas As regards the diet, all food-stuffs may be listed according to their action on the large intestine At one end of the list are such substances as white flour, on the other end is cabbage Between these extremes all the food-stuffs may be arranged Therefore, we must try out the various food-stuffs, starting at the bottom and building up, being guided in our additions by the response of the colon as indicated by the type of stool and the distress which the patient experiences

The mechanism of the distress is an interesting question We know that these patients have unduly active colons, and that they have a distress which can be recognized as being associated with this overactivity of the colon There is reason for feeling that the distress is associated with abnormal colonic contractions, but just what the mechanism is we are not as yet in a position to say

At this point I should insert a word of warning The symptoms and findings that I have described are those of a functionally deranged colon This may occur as a result of those factors just mentioned They may also be the result of a more serious, cause such as carcinoma, where the patient, owing to increasing constipation, has been irritating the large intestine by the use of severe purgatives And there are other pathologic conditions as an etiologic source, such as tuberculosis Therefore, be thorough in all your cases and do not overlook serious pathology

This type of case is not new It is among the most common

which you will have to meet. The symptoms are well known to all, and these cases have gone under the diagnosis of hyperacidity, hypo-acidity, gastric neurosis, gastric catarrh, chronic intestinal indigestion, flatulence, neurasthenia, and many other names. The causes given are even more numerous than the diagnoses, but the tendency in the past has been to incriminate the stomach as the seat of the trouble and to attempt to treat that. It is only within a short time that it has been recognized that the colon was the organ to show disorder of function. This opens a new means of approach for the study and treatment of this very large group of cases suffering from abdominal complaints.

The recognition of the fact that the colon is very often associated with the common symptoms of so-called indigestion is of the greatest importance, for it is opening to us a new approach to the solution of what has been a most unsatisfactory field of medicine from the point of view of diagnosis. At present we are only on the margins of this field. We know nothing about the physiologic pathology of what is going on, but it is to be hoped that the new means of approach may open the way to a better understanding of this type of case.

CLINIC OF DR CHARLES H LAWRENCE

EVANS MEMORIAL HOSPITAL

THYROID FAILURE WITHOUT MYXEDEMA*

Presentation of Cases Illustrating a Clinical Type of Hypothyroidism Not Usually Recognized Discussions of Etiology, Symptoms, and Laboratory Findings Results of Treatment Discussion

THE patients whom I wish to present illustrate a type of thyroid failure which differs so markedly from myxedema that the correct diagnosis is usually unsuspected. The clinical picture of myxedema is so strongly associated in our minds with mental and physical torpor, loss of hair, and the presence of pads of pallid fat, that it hardly occurs to us to suspect hypofunction of the thyroid when these symptoms are absent. Yet during the past twenty-three months we have seen 32 patients in this clinic who had none of these symptoms, but in whom the laboratory findings were identical with those in cases of myxedema, and the results of treatment with thyroid extract were so striking that there can be no doubt as to the common etiology of these two clinically dissimilar conditions.

The reason for this clinical dissimilarity lies, I believe, in the age periods in which the thyroid failure occurs. Failure in adult life, after growth has ceased, produces myxedema. Congenital or intra-uterine failure causes cretinism. It is failure during childhood or adolescence that produces, I believe, the clinical picture illustrated by the patients to whom I now call your attention.

Case I—This patient, a woman forty-two years old, has been under my care for the past six years. She came for relief of headaches which she said she "had always had." She can re-

* Evans Memorial Publication, No 78, A, 39

member definitely that she had them as a small child. They began usually at night, with nausea and chilly sensations accompanying their onset. The pain appeared first in the occipital region, spread forward around the head, and at the height of its severity was most marked in the temples. For twenty-four hours the patient was incapacitated. The pain then disappeared rather rapidly. The attacks occurred, roughly, every three weeks, but she had had intervals of three months between them. Properly fitted glasses had afforded no relief.

One sister has similar headaches, but they occur only occasionally. Two other sisters, three brothers, and her father and mother are free from headache, nor could I obtain a history of headaches in grandparents. The father, now dead, had attacks of angina pectoris. It is interesting that the sister who had similar headaches developed thyroid failure two years ago, a year after moving to Ohio. She developed typical signs of myxedema, and on examination had a basal metabolic rate of -22 per cent. In her case the thyroid failure did not occur till adult life had been reached, and the picture produced was typical myxedema.

The patient's past history is singularly free from definite incidents. She has never had any serious illnesses, and escaped mumps and scarlet fever in childhood. She never remembers being sick, as were her brothers and sisters, nor does she believe she was ever as well as they were. She states that "things always took it out of her more than the others." She never had the high spirits and vitality that other youngsters had, and though her appetite and digestion were good, she was always painfully thin. She matured at twelve. Her periods were regular, as a rule, occasionally two or three days early. They have always lasted five days, the amount has been normal, and there has never been any pain with them. The headaches were apt to occur at about the time of the periods, but this relation was not constant.

In spite of her handicaps the patient stood well in school, graduated from college, and at the time I first saw her was filling acceptably a position of responsibility which required initiative and executive ability. She was, naturally enough, depressed

about her future, for her headaches were increasing in frequency and severity, and she was "always tired." Her appetite was good, her bowels, previously always regular, were becoming constipated, and she found it hard to get to sleep because she worried about her ability to continue her work. The history is otherwise negative.

Physical examination at the time of her first visit gave few positive findings. The patient is a tall, thin woman, measuring 68 inches in height and weighing, then, 105½ pounds. Her skin was pale, cool, but not strikingly dry, the mucous membranes were normal in color. Her expression and posture expressed fatigue. There was nothing else remarkable about her appearance. Her hair was normal in texture, amount, and distribution. Her teeth were well kept, throat not remarkable. There was no enlargement of the thyroid and no adenopathy. The chest was symmetric, the breasts underdeveloped. The examination of the thoracic and abdominal viscera disclosed nothing abnormal. The extremities were not remarkable. There was no edema, no abnormal pigmentation. The eye-grounds and visual fields were normal. In cases of pituitary enlargement, the visual fields show a characteristic change in the great majority of cases, so the presence of normal visual fields is an important bit of evidence in the differential diagnosis of the causes of headache.

The usual laboratory examinations showed a normal blood-picture and normal urine findings, with the exception that a slight trace of sugar was reported at one examination. There was, however, no hyperglycemia.

The only diagnosis I could make on the evidence available was migraine. The patient was seen by several other physicians at different times during the next two years without benefit to the headaches. The only measure which brought any relief was curtailment of her activity to such a degree that it made an invalid of her. If she expended little or no energy, her headaches were fewer and less severe, but if she led a life that was anywhere nearly normal, no treatment influenced the frequency or severity of the headaches.

In March, 1923 the patient was admitted to this clinic for a week's study. The physical examination was unchanged. The blood-picture was normal, with the exception that lymphocytes comprised 55 per cent of the white cells. The white cell count was 6750. Routine examination of the urine showed no abnormal constituents. The phenolsulphonephthalein test showed that 51 per cent of the dye was eliminated in two hours. Clinical examination of the blood showed

	Mm. per 100 c.c.
Non-protein nitrogen	41.7
Urea	16.9
Uric acid	3.8
Creatinin	2.1
Sugar	86.0

The alveolar carbon dioxide was 34 mm., a low normal value. The sugar tolerance was normal, as determined by galactose. The urine and blood urea curves showed a sharp rise and delayed excretion.

The basal metabolic rate averaged -30 per cent on two concordant estimations. The temperature was 97.6° F., the pulse 75. The blood-pressure was constantly slightly below normal.

X-ray examination and examinations of the eyes and ears, including the Bárány test, revealed no pathology. The Wassermann reaction was negative.

Our findings left no room for doubt that the patient suffered from hypothyroidism. They also suggested that there was early renal impairment. The non-protein nitrogen, urea, and creatinin values are all slightly above normal, the blood and urine urea curves are similar to those found in nephritis, and the phenolsulphonephthalein elimination is at the low border of normal for the patient's age. Which of the two conditions was responsible for the headache could only be ascertained by observing the results of treatment separately.

The patient was therefore given thyroid extract, 3 grams daily, and no change was made in her diet or mode of life. Two months later the dose was diminished to 2 grams daily because her pulse-rate was at times a little rapid. She has continued this dosage, with brief interruptions, to the present time. She

has had only two headaches in the past twenty-three months. One of these came after an abnormal demand upon her strength, the other after she had had no thyroid for six weeks. She has gained $11\frac{1}{4}$ pounds in weight.

At the present time her appearance does not suggest malnutrition. True, she is still under ideal weight, but her skin is normal in appearance, her posture and expression are those of a healthy person. She has lost her depression and is full of interest and ambition.

A repetition of the laboratory examination gives some interesting information. The urine is normal. The lymphocyte count has fallen to 34 per cent. The results of the chemical examination of the blood are as follows:

	Mgm. per 100 c.c.
Non-protein nitrogen	30.0
Urea	15.0
Uric acid	3.6
Sugar	91.0

These findings are all normal.

The blood-pressure is 120/80, temperature 98.6° F., pulse 72. In short, the result has been a return to normal all along the line under the influence of thyroid medication. The last basal metabolism estimation showed the rate to be plus 26 per cent, and the patient was advised to stop her medication for a week. There were, however, no signs of hyperthyroidism.

I have shown you this patient because she represents a type of thyroid failure which has not been thoroughly described, and which, therefore, often goes unrecognized. Yet the condition is not extremely rare. We have seen 32 cases of it in this clinic in the past twenty-three months. The majority of the patients have been treated by several physicians, and none has recognized their condition as due to thyroid failure, probably because myxedema is absent.

Even without that condition, however, there are certain symptoms and signs which should raise the question of hypothyroidism in our minds. Extreme fatigability, for which there is no adequate explanation in the patient's mode of life or physical

examination should always raise the question of the level of thyroid function. If the stained specimen of blood shows no evidence of anemia, but does show a lymphocytosis, if the pulse-rate is below 70, and does not quicken much after exercise and if the temperature is subnormal it is unfair to the patient to omit from the examination a proper estimation of the basal metabolic rate. It is likewise unfair and dangerous to give thyroid because of the presence of these findings unless the basal rate is below normal.

The second patient whom I wish now to show you illustrates the results of long-standing thyroid failure of the kind just described

Case II.—This woman is fifty-three years old, single, and teaches school. She likewise complains of being tired all the time, and of headache and constipation. At twenty, she had measles and has worn a wig ever since because her hair, always fine, became so scanty. She has had no other serious illness.

She is, as you see, a tall, rather thin woman, who looks tired and depressed. Her skin is unelastic, but not thickened. There is a very slight symmetric enlargement of the thyroid. Her blood-pressure, two months ago, was 110/80, her pulse 68, her temperature 97.8° F. The basal metabolic rate was then -24 per cent. The radial arteries are thickened, and examination of the retina shows arteriosclerosis there. The urine has been of persistently low gravity, but shows no albumin or casts. In short, this patient has well-marked arteriosclerosis associated with hypothyroidism. The frequency with which these two conditions are found coexisting was pointed out by Falta¹ ten years ago.

Our experience in this clinic suggests that the arteriosclerosis is the result of the deranged protein metabolism existing over a considerable period of time. It will be remembered that the blood chemistry in Case I suggested renal impairment, but that under treatment the findings returned to normal. If such abnormal conditions persisted for many years, it is conceivable that they might be the cause of arterial degeneration.

In this second patient who is older, treatment has normalized the basal metabolism, but the arteriosclerosis persists and there is much less subjective relief than the first patient obtained. Her thyroid failure has been compensated, but her general nutrition still suffers because of the circulatory pathology. This is one reason why the results of treatment are not brilliant in some long-standing cases of hypothyroidism, and it likewise emphasizes the necessity of recognizing and treating that condition, since untreated thyroid failure is almost certain to result in degenerative changes in the circulatory system, which are irreparable. There are other degenerative changes which respond to treatment if it is instituted early, but become fixed in time. Roughly, 16 per cent of the patients with thyroid failure whom we have examined in this clinic show impaired hearing, which is benefited, if the damage is not of too long standing, by treatment with thyroid extract.

This question of the treatment of thyroid failure is not, perhaps so simple as it sounds. The degree to which basal metabolism is depressed is not a reliable index of the amount of thyroid which must be given. There seems to be, especially in patients with long-standing deficiencies, an initial inertia which it may require large doses to overcome. The basal metabolic rate in these long-standing conditions is often not so low as in others of lesser chronicity. Therefore the individual requirement of each patient cannot be calculated beforehand, but must be carefully worked out. The dosage required to raise the metabolism to normal is usually greater than that required to maintain it at normal after it has reached that level.

Until the basal rate has been normalized, and the subjective symptoms show improvement, the patient should be seen at least weekly, and a record of pulse-rate, temperature, weight, and subjective symptoms must be kept. If possible during this period the basal metabolism should be estimated at weekly intervals, so that its response to the dosage given may be ascertained. As the metabolism nears normal the dose of thyroid extract should be diminished (usually about one-third), and when the metabolism and pulse-rate have become stabilized at the

normal level, the patient may safely be seen at increasing intervals. Inasmuch, however, as functional activity of the thyroid fluctuates considerably under the influence of fatigue, nervous strain, or infection, the patient should be educated to report any of these events promptly. It will then be advisable to "check up" on the basal metabolism, and it is often necessary to revise the dosage of thyroid extract. Pregnancy, if it occurs, has a marked effect on thyroid function, and every pregnant woman whose thyroid is below par should be closely watched throughout the pregnancy and the period of lactation. My experience with pregnancy complicating thyroid failure is small, for the latter condition seems to be usually associated with sterility, but in the few cases I have observed it required an increased amount of thyroid extract to maintain the patient at a normal level during pregnancy. Knaus² in a recent article states that there is diminished function of the thyroid during pregnancy, as shown by characteristic changes in nitrogen and chlorid retention and a lowered iodine content of the colloid.

As a rule, I use thyroid extract rather than thyroxin in the treatment of these patients. I feel that there is less danger of producing toxic symptoms in case the patient fails to report as frequently as requested. Moreover, our experience in 2 cases has made me feel that the two preparations do not have an identical effect on the human metabolism. Both the patients I refer to showed high normal blood-sugar values before treatment, and both, while taking thyroxin, developed glycosuria and hyperglycemia. The substitution of thyroxin was accompanied by disappearance of the condition in each instance, but it reappeared when thyroid extract was resumed. It seems certain, therefore, that thyroid extract may have effects which thyroxin lacks, and since we are supposedly treating a failure of the entire thyroid secretion, the extract of that gland seems the more logical answer to the average patient's needs.

Thyroxin is, however, a most valuable preparation in those cases in which thyroid extract does not give satisfactory results. In my experience it is less likely to cause nervousness. It is ideal when quick results are necessary, but it should be used only

when the patient can be observed frequently and continuously. Such a "high explosive" must be constantly watched and carefully used.

I do not want to leave the impression that the entire treatment of these patients consists in giving them the proper amount of some thyroid preparation. As strength and energy return, they are prone to overdo, and they must be educated to increase their activity slowly, so that they may re-establish that reserve which is the foundation of good health. Elimination of focal infection is most important, and should be insisted upon as essential to recovery. Lightening the load wherever possible, whether by correction of eye-strain or elimination of domestic friction, accelerates recovery. Many of these patients have mental depression, many are irritable and uncoöperative. These symptoms disappear under treatment, but due allowance must be made for them when present. There is a reason for these symptoms in the deranged metabolism and nutrition, and the patient should be defended from the impression that she is "neurasthenic."

After a patient has regained normal health, the question is usually raised as to the necessity of continuing treatment indefinitely. I have never seen a patient with definite thyroid failure who was eventually able to get along without thyroid, but it is often possible, after a time, to omit medication during regular intervals. The first patient I showed you has gone without thyroid extract for a month at a time without ill effects, but when, after eighteen months' treatment, she attempted to omit it for six weeks, her headache and depression returned suddenly and violently. I believe it is advisable to omit medication from time to time, for it minimizes the danger of producing hyperthyroidism.

The danger of producing artificial hyperthyroidism in these patients is a very real one. When they have enjoyed normal existence for a year or more they are apt to forget to keep in touch with their physician. They feel that thyroid extract is their salvation, and so go on taking it, without proper control, until suddenly a thyroid explosion occurs. For this reason it is

wise to omit medication for stated intervals after normal health is well established. If this results in the return of symptoms, the patient will be quick to report them.

In conclusion, I wish to briefly emphasize certain points that I have tried to illustrate. These are:

1. Thyroid failure of marked degree may exist without causing myxedema.

2. The condition is frequently overlooked because of the absence of signs usually associated with hypothyroidism.

3. The symptoms of fatigability, irritability, and depression are often called neurasthenia. That diagnosis should not be made nowadays until the patient's metabolism, basal and special, has been thoroughly tested and evaluated.

4. Thyroid failure without myxedema is a definite clinical type, due to failure of normal secretion before maturity, possibly before puberty.

5. Fatigability in a patient showing no organic disease and no adequate anemia, but showing bradycardia, subnormal temperature, hypotension, and an increase in the number of lymphocytes in the blood, should raise the suspicion of thyroid failure.

6. The administration of thyroid extract is not, however, justified by the presence of those findings, and should not be instituted until the true basal metabolic rate has been determined. In doubtful cases, in which the rate is between -10 and -20 per cent, determination of the sugar tolerance is the most useful diagnostic aid. Slight thyroid failure does not effect sugar tolerance.

7. Thyroid extract and thyroxin are highly potent, and therefore dangerous preparations. They should never be given unless thyroid failure has been proved to exist, and their administration demands close oversight of the patient until their effect has been determined.

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CLINIC OF DR H ARCHIBALD NISSEN

ROBERT BRECK BRIGHAM HOSPITAL

SOME OBSERVATIONS ON ARTHRITIS

THIS article is an attempt to record four observations of arthritis

1 Usually it is impossible to determine the condition of a joint by inspection, palpation, and functional tests

2 A study of x-ray plates of joints shows that frequently three distinct types of joint, bone and tissue changes may be demonstrated, and these may be named hypertrophic, atrophic, and infectious arthritis

3 Not uncommonly a study of spines by x-ray will show marked increase in bone formation of the vertebræ, with lipping, deformity, etc., and these changes may not be suggested by other examination than the x-ray studies. These changes may and can explain the reasons for the presence of various pains and aches in different parts of the body. These disturbances may simulate other diseases

4 Possibly the majority of diets suggested for the treatment of arthritis are fallacious

The photographs of hands and the accompanying x-ray plates show somewhat, that externally the hands are similar but the x-ray plates show an entirely different internal structure than one might expect to find present

Among the arthritic patients at the Robert Breck Brigham Hospital and those seen in private practice a number of observations have been made which have been of value apparently in diagnosis and prognosis. Some of the patients at the Robert Breck Brigham Hospital have been under constant observation and study for years. Most of these patients have represented the more advanced stages of arthritis. A large part of the

various studies have been of negative value and, therefore, by exclusion are of considerable value. One fact which has been proved repeatedly is that one cannot judge or estimate accurately the amount and extent of joint damage by inspection, palpation, and functional activity in the majority of patients.

The above statement demands some plan of classification of arthritis, a simple plan and one easily demonstrated. The photographs of hands and their corresponding x-ray plates



Fig 257 —x-Ray of normal hand

write their own classification in a way. The external appearances of the hands reveal some differences, which the photographs show much less clearly than the living hand. However, enough does show that can be pointed out to illustrate the differences.

The first plate is a copy of the x-ray plate of a normal hand (Fig 257). A close study of the plate presents the following details. First, attention should be directed to the soft tissue

parts of the hand as well as to the detail of the bones. Notice particularly the very faint outline of the soft structures surrounding each joint. This will give one an idea of the normal appearance of the soft parts in these locations. Then notice the appearance of the articulating surfaces of the bones, the clean-cut outline of the joint surfaces, and the narrow white line which may be said to represent cartilage, and study also the definite spaces between the articulating ends of the bones. A study of the bone tissue itself shows the outline of each bone and very clearly the cortices. The trabeculations are very well marked

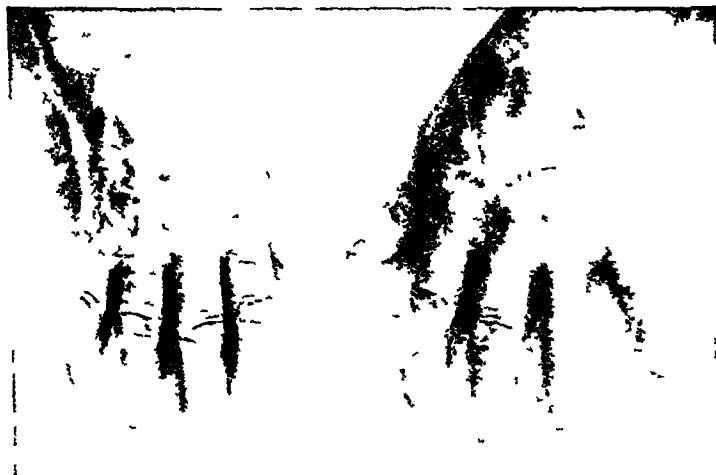


Fig 258—Photograph of hands of elderly woman

If the *x*-ray plate is studied as a whole the articulating ends show a lighter shadow than the shafts of the bones. The appearance of the carpal bones have clean-cut outlines with each bone showing its trabecular configuration.

The second and third illustrations are the hands and *x*-ray plate of a woman seventy years of age (Figs 258, 259).

A study of Fig 258 shows very little apparent deformity except for the slight prominence of the terminal phalangeal joints. These appear to be very slightly deformed. The appearance of the tissues about the nails shows a moderate heaping-up. The skin retains its normal markings and thickness.

If Figs 258, 260 are compared these observations are seen more clearly. The third illustration (Fig 259) tells a very different story because there is definite thickening around each joint, the terminal phalangeals show more of a fungus-like form than was seen in Fig 257. The periosteum is less clearly marked generally. The edges of the articulating surfaces show proliferations of bone, making spur-like projections. The trabecula-



Fig 259 — x-Ray of hands shown in Fig 258

tions are less clearly defined. The shafts are denser and thicker and the periosteum presents a shag-bark appearance. The white zones are also present, but narrower, at the articulating ends. The spaces between the joints are slightly narrower. There is more uniformity in the entire density of the bones. The carpal bones are denser generally, but they retain their lines of cleavage fairly well. In this group the increase in bone and the apparently

slight change in the joint may be well termed "hypertrophic arthritis"

This type of arthritis is not apt to be found in individuals under forty-five, and those having these changes are apt to be of the heavy-boned type, stocky build, and having a wide rib spread

Hypertrophic arthritis is not a normal finding in people of middle and later ages, although it may be present for years, slowly progressing until finally the patient complains of symptoms suggesting arthritis, but so vague they may be due to other



Fig 260 —Photograph of hands of middle-aged woman

causes When the hypertrophic changes are present there may be no symptoms until there has been a strain, chilling of the body, wrench, sprain, infection elsewhere in the body (as a bronchitis) fatigue exhaustion Finally, without apparent cause, symptoms occur, ushered in as swelling, pain, stiffness or increase in hitherto unnoticed deformity of the hands or other joints The manifestations in the joints may be transitory or chronic, with exacerbations and after once appearing tend to recur more readily The pain may be dull, sharp, constant, intermittent, localized, diffused, or referred

The fourth and fifth illustrations (Figs 260, 261) show the hands and x-ray study of a woman thirty-five years of age. The photograph of the hands presents the following characteristics. The skin over the middle and distal phalanges shows a thinning, with a partial loss of the normal markings, giving a slight glossy sheen to the skin early in the course of the symptomatic stage. Later this atrophy of skin will become very much

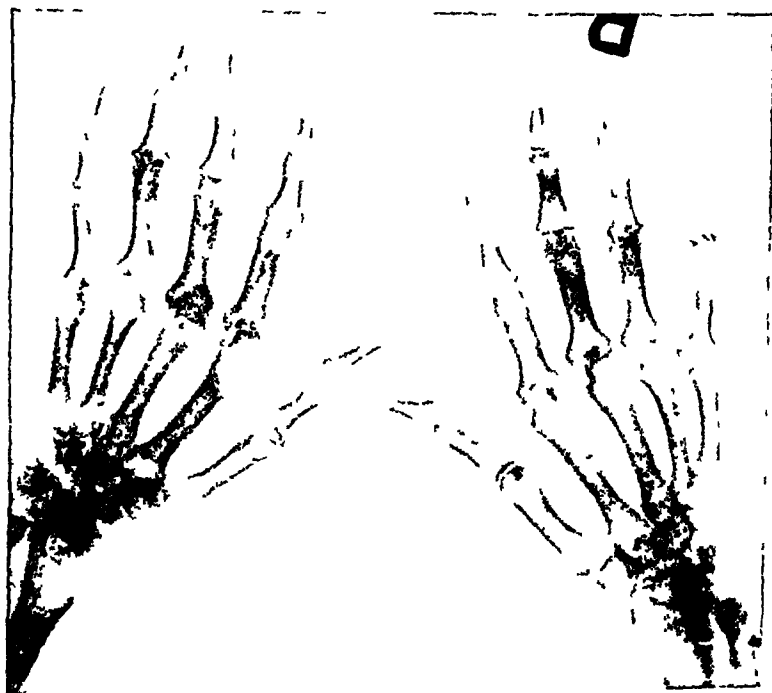


Fig 261 —x-Ray of hands shown in Fig 260

more marked, so that all of the markings tend to disappear and there is left a shiny isinglass-like skin. The terminal phalangeal joints in this particular instance show no changes on inspection, palpation, or motion, but the x-ray plate shows a definite narrowing of the spaces between the articulating ends. If this plate is compared with the first one, this difference is more noticeable. The middle phalangeal joints show some apparent

swelling and deformity, however they present a fair degree of flexion and extension, and one might say that the joints were only slightly impaired, but the x-ray study tells an entirely different story. The joint spacings and markings are practically absent in the third phalangeal joints of each hand. The other middle phalangeal joints show marked narrowing and a fair degree of loss of normal markings. The phalangometacarpal articulations show crowding with a narrowing of the joint spaces and destruction or loss of bone tissue. The general impression of the hands is one of general loss of lime salts, destruction of cartilage, and a mushroomed effect produced by crowding of the articulating ends. Carpal bones are crowded and the boundaries are almost erased. The bones show a marked loss of lime salts.

This type frequently progresses to marked deformity, ankylosis, and severe loss of bone substance.

The important points in this instance are that inspection, palpation, and motion do not give one any clear idea of the marked amount of actual damage and bone loss which is present. The patient, whose plates are shown, first noticed swelling and stiffness of her joints five years ago, later there was deformity. When first seen this was marked and the joints appeared to be ankylosed. The x-ray plates at that time revealed fewer changes and less loss of bone and cartilage than is shown above but after a year's treatment her hands present much less deformity, fair motion, and little swelling, and she is earning her own livelihood at work, although the x-ray studies at present show even greater loss of bone tissue than at first.

This demonstrates that whereas examination of a joint may show one thing, the x-ray plate shows another.

The general impression of the x-ray plate (Fig 261) indicates atrophy of bone with destruction of joints, which writes its own description of atrophy, and so may be well termed "atrophic arthritis."

This type of arthritis appears to be found most commonly early in life that is, between thirty and forty years of age. The type of individual having this form is apt to be of the slender build, small bones, and with a narrow rib spread.

The sixth illustration (Fig 262) is an x-ray plate of a third type of "joint" involvement which is very common, and not infrequently called arthritis. A study of the soft tissue shows an increased density about some of the joints and the outlines of the digits show slight bulging, particularly of the middle phalangeal joints. On inspection these hands show during the first attack very slight or no changes in the skin,



Fig 262—x-Ray plate showing "infectious arthritis"

but as time goes on, if there is no abatement in symptoms, and if there is much fluid in the joint and much swelling in the tissue surrounding the joint, atrophy may be produced because of the increased pressure. (Fluid may be increased in the joints of any one of the various types of the arthritis described in this paper. By itself it is not an index of any one joint involvement.) This may simulate the atrophy of atrophic

arthritis, but the other changes mentioned as present in atrophic arthritis are less apt to be found

The atrophy so produced is more like the atrophy of disuse, whereas the atrophic arthritic shows actual loss of bone and general thinning. This type is really a peri-arthritis, a peri-articular involvement. It is more apt to be found in the young adult, but may be present in an individual who is atrophic or hypertrophic as well.

The above illustrations present three types of joint involvement. These may be termed "hypertrophic," "atrophic" and "infectious arthritis." These illustrations have been selected with particular care to avoid the extreme stages of the three types of arthritis, because after all it is in the "early" case with apparently slight or no external deformity that we should be most interested. The late stages offer very slight chance for more than partial relief at best, although here, too, the x-ray study may reveal a condition amenable to treatment.

The hypertrophic and atrophic arthritis patients show their distinctive bone changes from the first and retain their different developments throughout the course of the diseases. The term "early" is used to denote the time the patient consults his physician for the first time, or that period which the patient declares to be the first appearance of symptoms or signs of joint disturbance. This means the onset of swelling, stiffness, pain, creaking, or impaired function. This "first appearance" is often a late appearance.

The other types of joint involvements may be classified as a manifestation of a recognizable disease process, i. e., gonorrheal arthritis is part of gonorrhea, tuberculous joints are a part of tuberculosis, Charcot joints a part of syphilis, septic joints a part of sepsis, etc.

The three types of arthritis discussed and illustrated as hypertrophic, atrophic, and infectious do not appear to be parts of any specific disturbance. In fact, no one definite causative agent has been found constantly in any one of the three types.

The three types as presented show definite structural changes which, when examined carefully, usually classify themselves

into the three distinct groups, and a study of these groups shows certain constant common factors peculiarly typical of each type

To repeat, inspection, palpation, and functional test of joints may at times give accurate information of the true state of affairs, but often one cannot be at all certain, and irrespective of the external appearance of the joint, careful x-ray study, particularly serial x-ray plates, is indicated. Such study will show certain fairly constant characteristic structural changes which



Fig 263 —x-Ray plate showing deformity with no symptoms

mechanically separates arthritis into three groups—increased bone formation or hypertrophic arthritis, loss of bone and destruction or atrophic arthritis, and a periarticular impairment at times involving joints, or infectious arthritis

Serial x-ray studies of spines, physical examinations of backs, accidental or coincidental x-ray studies of spines have demonstrated several interesting observations

Figures 263 to 266 show different degrees of bone formation. Figure 263 is a plate taken of a patient having kidney stone

There were no symptoms pointing to arthritis of the spine, but it shows marked bone increase which is an outgrowth from the vertebral body. This is the type of hypertrophic arthritis which may be present for years with no symptoms until a strain or wrench, etc., produce an increased congestion of surrounding tissues, which, coupled with the bone hypertrophy, suffices in some manner to produce nerve irritation. The site of the bone change may determine the character of pain produced by pressure on the particular nerve or nerves in this location. This pain

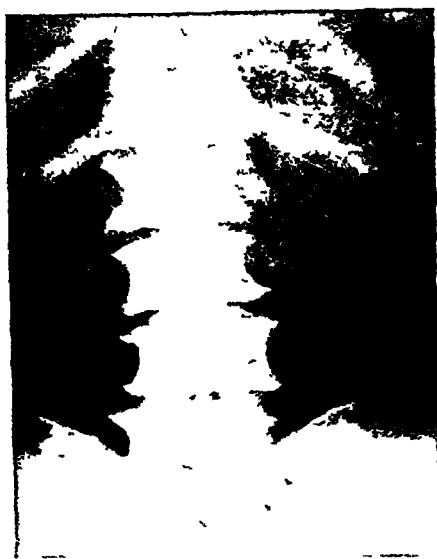


Fig 264—x-Ray plate showing slight deformity with symptoms

may be of diverse character and localized to one spot or radiating. It may be constant or intermittent and may involve practically any part of the body. It thus may simulate part of the picture of various other diseases, although inspection and palpation of the back may reveal nothing abnormal.

Where there have been x-ray plates of the spine taken several years apart there may be revealed no change in the amount of bone formation. The difference lies in the development of symptoms, so that one may say it is not necessarily the

degree or amount of bone change which produces symptoms when the spine is involved, but that there is something more. This "something more" may be activated by the various causes enumerated—strain, etc—or occasionally the increase in bone formation may progress to the point where it alone produces symptoms by pressure or limitation, but the actual exciting producer of symptoms appears to be congestion of soft parts



Fig 265—x Ray plate showing attempts at immobilization

about the spine, such as wrench, sprain, exposure, etc., and the symptoms subside as the congestion subsides, but they tend to return on subsequent occasions

Figure 264 is of a spine which presents much less bone hypertrophy, but symptoms were present and very marked. This observation is of value in that it demonstrates that even slight hypertrophy of the spine with congestion, irritation, infection

elsewhere may produce marked symptoms of lameness, pain, limitation of functional activity, and still very little bone change may be present

Figures 265 and 266 show how ankylosis does occur, producing in some instances elimination of symptoms, and presents merely an ankylosis of the spine. It also shows nature's attempts to produce a more equal distribution of stress in the presence of misalignment.

Curiously, and yet naturally, there is very little symptomatology in the atrophic spine, although the same possibilities of



Fig 266 —x-Ray plate showing response to stress

stress and strain are present. The chief things to emphasize from the above statements—that where symptoms of pain and irritation occur in middle-aged people the possibility of arthritis of the spine should be remembered and ruled out as a causative factor if the clinical picture of the supposed disease is not complete. Because due to the nerve irritation, direct or indirect or by actual pinching of spinal nerves at points of exit, or from

increased pressure in the vertebral canal, or by increase and density of the articulations about the spine, leg, arms, etc., the pain may be present constantly or intermittingly, and if present in the lower right quadrant and presenting on superficial or deep pressure, tenderness, a diagnosis of "chronic appendicitis" is made, particularly if constipation or indigestion is present

The nourishment of an arthritic or "joint" patient is an individual affair. At the Robert Breck Brigham Hospital patients have been kept on various diets, not for days but for months and years, and the practical observation has been that there are no marked demands for abnormal food intake.

The physiologic demand intake has met all requirements as a measurable balance, that is, enough food to meet the patients' body demand, and this means a well-balanced food mixture. By this is meant sufficient carbohydrate to maintain 1 gram to 3 grams per kilogram, $\frac{1}{2}$ to 1 gram of protein per kilogram, and 1 gram fat per kilogram of body weight.

The kind of food whenever possible is the fresh food, as fresh vegetables, fresh meat, milk, eggs, cheese, butter, entire grain breads, a moderate amount of fresh fruit, as orange or grapefruit, and simple desserts. Such a food mixture meets all mineral, salt, vitamin, carbohydrate, protein, and fat demands of the body.

Individual modifications have to be made. One patient is demonstrably worse if certain foods are eaten, then omit that particular food from that patient's intake, but not from all arthritics' food intake. The foods should not be highly seasoned. An excess of sugar in some patients seems to make them worse. Generally speaking, the individual has to have his metabolism maintained.

Meats for "uric acid" notions, "minerals with increased calcium formation," and similar fancies have failed to show any justification for acceptance.

If sufficient food in a balanced manner is given, eaten slowly, no effect of a deleterious nature has been proved to result in any of our patients.

Excessive purgation and pernicious use of laxatives is con-

demnable in all arthritics Here again the individual must be treated Some patients with dilated sluggish cecum and atonic intestines must be treated accordingly On the whole, the arthritic should be treated as an individual who for some reason has become unbalanced structurally and shows joint changes He should be built up, nourished, and exercised

CLINIC OF DR RAPHAEL ISAACS

FROM THE MEDICAL SERVICE OF THE COLLIS P HUNTINGTON
MEMORIAL HOSPITAL OF HARVARD UNIVERSITY

BACKACHE IN DISEASES OF THE LYMPH-NODES

IN the clinic today we will consider 2 patients, both of whom have suffered from severe backache. As the diagnosis in the one case was not as evident at first sight as in the other we will consider it first.

Case I—This patient is one whose presenting symptom is severe backache of six weeks' duration. The history is briefly as follows:

History of Present Illness—The patient is a motorman, fifty-eight years of age, a Canadian by birth. During the course of his work about two years ago he noticed that he was "run down" and he felt in the need of a vacation. This was accentuated by the death of his wife at that time. He continued at his work, although he had to force himself to do it. The most marked symptom was the ease of fatigue. This continued for about a year, when he noticed that he was becoming paler and was losing weight. About six months later he caught a "cold" and developed symptoms of malaise and weakness which were called "old-fashioned" grip. He went to a hospital for observation, and, during the course of the examination, it was noted that his spleen was larger than normal. Recovery from this attack was slow, and he rested at home for two months. During this time he noticed a "lump" about the size of an egg in the right groin. No structures that suggested enlarged lymph-nodes had been noticed previously. The mass was not painful, and there was nothing that suggested that he had any infection of his leg to

account for it. The swelling slowly subsided and several small nodules remained. He returned to work six months ago, somewhat improved, but still feeling below par. A symptom which bothered him off and on was itching of the skin of all his extremities and trunk. This necessitated scratching and produced crusted lesions. In the course of this past year of ill health he has lost 25 pounds in weight.

He continued at work until about five months ago, when he developed a pain low in the lumbar region. This was dull and aching in character, localized in his back, and did not radiate. He noticed that when lying on his right side he obtained some relief, but on rising to a sitting position the pain was accentuated. There were no associated gastro-intestinal or genito-urinary symptoms. The pain continued rather persistently for about two weeks, during which time the patient had his back rubbed, and he gradually improved. He resumed driving his electric car, but still experienced a dull pain in his sacro-iliac region, with a sharp "catch" at times. The pain soon became very severe and he was again forced to give up his work three months ago. The pain became most marked in the right sacro-iliac region, radiating round the crest of the ilium, and passing down the anterior aspect of the right thigh to the knee, sometimes lower (Figs 267, 268). The intense pain felt "like the muscles were being pulled off the leg." He could not stand on his right leg. About a week before he entered our clinic, which was three months ago, the pain shifted from the right leg to the left leg, and the pain in the right sacro-iliac region became almost unbearable. He was confined to bed and could lie only on his right side, with his right leg extended and his left leg flexed. Any other position caused great suffering. Massaging, ironing, and heat gave no relief. It was in this condition that he was brought to our hospital in an ambulance three months ago.

Before giving the details of his physical examination a few points in his past history are of interest.

Past History—About thirty years ago he had an attack of acute rheumatic fever and was in bed for four months, with red, swollen, and painful joints. He had tonsillitis some twenty

years ago and had his tonsils "snipped" at that time. He has had sore throats many times since. Before the age of twenty he had measles, scarlet fever, and mumps, with complicating orchitis. He has been troubled with dental caries and has had several teeth crowned. He has also had attacks of what he calls "bronchial catarrh," with a chronic, productive cough, and occa-

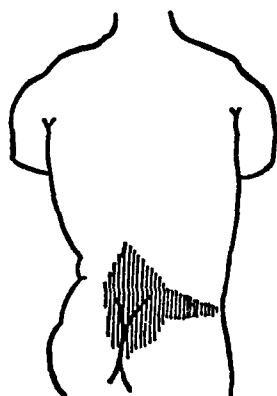


Fig 267 —Area of pain in the lumbosacral region

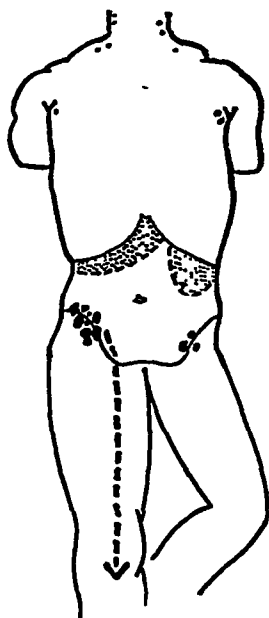


Fig 268 —Distribution of the palpable lymph-nodes. The dotted line shows the course of the pain which radiated from the lumbosacral region, around the crest of the ilium to the anterior inner part of the leg.

sional attacks of pain that have been called "pleurisy." He has never had his chest tapped. About two years ago he had some indigestion and distress within an hour after a meal and was troubled with a feeling of distention. His discomfort was relieved by eructation and the gastro-intestinal symptoms gradually disappeared.

Family History—His parents died of “shock” in old age. One sister died of “quick” consumption about twenty-two years ago. Four brothers and 4 sisters are alive and well. The patient knows of no one in the family having symptoms of disease in any way resembling his. Pernicious anemia was given as the cause of his wife’s death. Two children died in infancy, and two are alive and well. The patient’s habits have been good.

Physical Examination—On physical examination, when the patient was first seen in our clinic, twelve weeks ago, he showed a well-developed and well-nourished adult man, lying in bed, evidently suffering from considerable pain. One of the outstanding features was numerous scratchmarks and small crusts over the skin of his limbs and trunk. A few old purpuric spots were present over the anterior surface of the lower part of his legs.

His tonsils were small and ragged.

Of the lymph-nodes, the cervical ones were palpable, the largest being 1 cm. in diameter, but most of the posterior cervical chain and the supraclavicular nodes were not over $\frac{1}{2}$ cm. in diameter. They were not large enough to be noted simply by inspection. In the right axilla a small node $\frac{1}{2}$ cm. wide was palpated, and in the left axilla two nodes, one 1 cm. and one $2\frac{1}{2}$ cm. in diameter. There was a mass of nodes, about 7 by 5 cm., in the right groin composed of individuals varying from $\frac{1}{2}$ to 2 cm. in their greatest diameter, and a few somewhat smaller nodes in the left groin. All the nodes were discrete, elastic, and non-adherent to the skin, and non-fluctuant. They were not painful or tender on pressure, and the overlying skin was not reddened.

There was some loss of sensation in both legs, especially in the skin of the anterior and inner surfaces of the thigh, knee, and calf. No tenderness was noted over the nerve trunks.

The heart and lungs showed no evidence of pathology, and the retrosternal dulness was within normal limits.

The spleen was much enlarged, occupying the whole of the left upper quadrant of the abdomen, and extending $11\frac{1}{2}$ cm. below the costal margin in the nipple line, and reached a point $4\frac{1}{2}$ cm. from the midline. The surface was smooth, and a notch was easily felt. The spleen was not tender. The liver edge was

palpable 7 cm below the costal margin in the nipple line, and extended up through the epigastrium. The edge was regular and not tender. The examination was somewhat interfered with by the intense pain from which the patient suffered, and the inability or unwillingness because of fear to extend his left leg or turn from his right side. However, it was fairly evident that there were no areas along the spine itself that were especially tender on pressure, and the sacro-iliac joint gave no signs of disease. Rectal examination showed that the prostate was not enlarged or tender.

Further examination was not possible because the patient could not lie flat or extend his leg. It would have been desirable to have tested out his reflexes in greater detail and to note any areas of localized spasticity in the abdomen. An x-ray study of the spine would have been helpful in eliminating a bone lesion. For future study a lumbar puncture with withdrawal of fluid for examination was to be considered, and roentgenograms of the spine.

The blood at this time showed

Red blood-cells	3,900,000 per cu mm
Hemoglobin	77 per cent
There was moderate achromia and some variation in the size of the red corpuscles	
Leukocytes	9,800 per cu mm

The differential count of 400 cells showed

	Per cent
Poly morphonuclear neutrophils	62 0
Poly morphonuclear eosinophils	1 0
Small lymphocytes	19 0
Mononuclears	13 0
Atypical mononuclear cells	5 0

The Wassermann test of the blood-serum was negative.

The urine showed nothing abnormal.

During the period of his observation, which extended over several weeks his temperature varied between 100.2° and 98.2° F but there was no regularity in the variations from day to day. The pulse-rate varied between 100 and 80, with respirations varying around 20 per minute.

The problem presented by the case before us is to trace the cause of violent pain in the back, emphasized in certain positions of the body, and radiating into the legs. The first condition one thinks of is some form of arthritis. In the absence of a history of trauma, and with no tenderness on pressure over the sacro-sciatic region, strain of the ligaments seemed unlikely. The patient's age, fifty-eight years, and the immediate history, as well as the physical examination, were not suggestive of a tuberculous or typhoid lesion of the spine. An examination of the spinal fluid would have helped to rule out meningitis and possibly a cord tumor. The nerve tenderness of neuritis and the tender areas of sciatica were absent. The normal prostate did not suggest its implication in the etiology of the pain. The crowned teeth and the history of dental caries naturally suggested an arthritis or myositis associated with focal infection. There was no localized tenderness or signs to suggest a psoas abscess or an appendical lesion. One must not forget the referred pains of renal and biliary colic, but the continuation of the pain for several weeks and its alleviation in certain positions of the body makes a lesion of this type seem less likely, especially with the other signs. The enlarged spleen and liver and the palpable lymph-nodes and irregular fever suggested, among other conditions, lues, as well as lymphosarcoma, leukemia, Hodgkin's disease, or other form of malignant lymphoma. The negative Wassermann made syphilis seem unlikely. The absence of marked or progressive gastro-intestinal symptoms, the absence of involvement of the tonsils, the absence of subcutaneous lymph-nodules in unusual places, made the diagnosis of lymphosarcoma less probable, although it was to be considered. The blood-picture was unlike that of a typical leukemia, being more in accord with that of aleukemic leukemia, or pseudoleukemia. The biopsy of a cervical lymph-gland confirmed, on section and examination, the diagnosis of a form of malignant lymphoma of a type consistent with what is often known as aleukemic lymphocytic leukemia or pseudoleukemia, but not of a character considered typical Hodgkin's disease, with the pathology described by Dorothy Reed.

As we look back over the history the train of symptoms

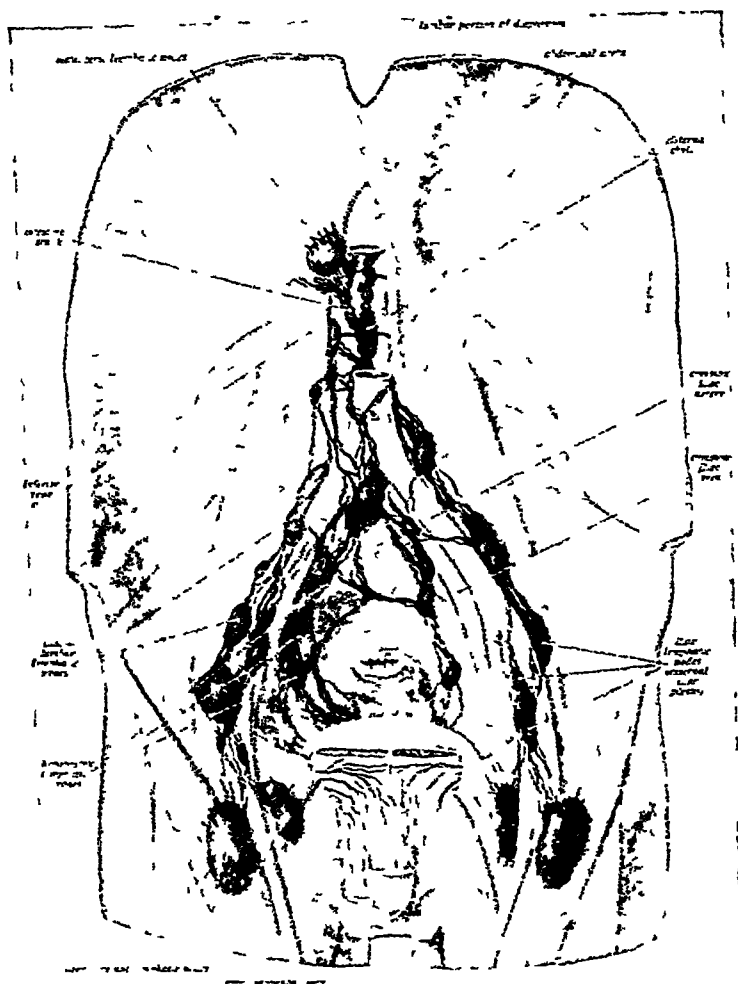


Fig 269 —Location of the principal lymph-nodes of the pelvis and the deep inguinal region, showing the relations of the surrounding organs which may be compressed when the nodes enlarge (Atlas and Text-book of Human Anatomy, Sabotta and McMurrich)

now becomes more connected The fatigue, loss of weight, and the itching were early symptoms characteristic of the disease

The attack of "grip," with the slow recovery, was quite probably a flare-up of the process which had been slowly progressing for at least a year and a half. At that time the splenomegaly was present and the lymph-nodes enlarged. The cervical group, however, never became prominent. Enlargement of the pelvic nodes, causing pressure on the nerves, followed, and can account for the pain and the partial loss of feeling of peripherally excited sensation in the regions from which the nerves led. In this case the affected areas corresponded fairly well to the distribution of the anterior crural nerves, with the involvement of some of the other branches of the first, second, third, and fourth lumbar nerves. The enlarged nodes must have been so situated as to allow the blood-vessels of the legs not to be involved, as no edema was present. In some cases the edema and venous stasis are prominent features of enlargement of nodes within the abdominal cavity. The only evidence of enlarged internal nodes that we had at the time was the enlarged inguinal nodes and enlargement of nodes elsewhere. We were not able to feel the pelvic nodes (Fig 269). Sometimes these are palpable through the rectum.

The treatment, therefore, consisted in removing or relieving the pressure. Because of the location of the nodes and their probable extent, their surgical removal was not feasible. Irradiation with the deep short-wave Roentgen ray offered the quickest method of relief, and four exposures on consecutive days were given to the pelvis anteriorly and posteriorly. After the third exposure the pain was much less, and after the fourth treatment the patient experienced no pain unless he moved. Fowler's solution was prescribed, and the patient returned to his home. His improvement continued very rapidly, and in two weeks he was able to walk. In about two weeks more only the slightest discomfort remained. The spleen then was smaller, extending down 10 cm below the costal margin in the nipple line, instead of 11½ cm, as before the treatment. The mass in the right groin had decreased, so that it measured only 3 cm in diameter, and the other nodes were about the size first noted.

In the course of the next three weeks he felt practically

normal This was two months ago During the period after the irradiation he gained 7 pounds in weight within a few weeks The only new symptom was nocturia (twice during the night), he had never been troubled in this way before This may have been a nerve pressure phenomenon or a direct invasion of the prostate by lymphoid tissue He volunteered the information at this time that normal sensation was returning to his knees, though some weeks prior to irradiation he could kneel on a sharp edge without feeling it

Some weeks after the patient had been relieved of his pain and was able to lie in any position a roentgenograph of the lumbosacral spine was made This showed definite hypertrophic arthritis with "lipping" of the edges of the vertebra If we had had this evidence in the beginning we would have been misled into thinking that the pain was a result of the hypertrophic changes in the bone If this were the case, it is improbable that the Roentgen-ray irradiation treatment would have relieved it so quickly The bone changes remained, but the pain disappeared It is quite possible that the enlarged lymph-nodes, pressing on nerves which were already irritated by hypertrophic changes in the bones, accentuated the condition, and thus increased the pain, which otherwise would not have been so marked

Today you may note that he looks like a healthy man in every respect He moves his body freely in every direction, and the relief-from the pain, which is so fresh in his memory, makes him very eager to go through all kinds of exercises just to emphasize how well he feels The itching, though less intense, still persists Now he feels no pain except on going to bed at night, when there is a dull discomfort in the lower part of the back Although the symptoms have been alleviated, the disease itself has not been affected The largest of the nodes on the right side of his neck now measures 1 by 2 cm, although previously the largest node was but 1 cm in diameter The spleen is a little larger than it was when he first presented himself, three months ago, extending down 12 cm below the costal margin in the midclavicular line The skin of the lower part of

the abdomen is much pigmented from the scratching, combined, probably, with the effect of the irradiation and possibly the arsenic, although it must be remembered that pigmentation is frequently a part of the disease. He is continuing taking Fowler's solution and will be observed from time to time.

The essential features of this case of malignant lymphoma are that the largest lymph-nodes were not in the neck, as textbooks picture in Hodgkin's disease and some other forms of lymphoma, but in the abdominal, pelvic, and inguinal regions. This location of such a process is probably more common than reports would lead one to believe, and seems to be frequently overlooked in the absence of enlarged peripheral nodes. Such cases are treated for rheumatism, sciatica, lumbago, neuralgia, forms of arthritis, and kindred diagnoses, often for a long time before the correct diagnosis is established.

As to the prognosis, the patient may be expected to suffer for varying periods of time, with relapse and improvement until the Roentgen rays or the rays of radium can no longer benefit his symptoms. Such treatment, however, must not be given at random, but cautiously, for too much can readily produce undesirable results. Symptoms are apt to be mostly mechanical in origin, but the constitutional element with progressive anemia is to be anticipated, and will gradually become more pronounced. One point at present is in his favor for fairly good health in the future, namely, that the red blood-corpuscle count after irradiation did not decrease, and during the course of the past few months his hemoglobin increased to 95 to 100 per cent. Definite leukopenia (4600 to 5400 leukocytes per cubic millimeter) has been present for at least two months following his x-ray treatment. Leukopenia in this disease is often a part of the clinical course in the later stages even without x-ray treatment. It may often become more marked, especially as the anemia becomes a more prominent feature. Roentgen-ray or radium treatment is unwise when there is a lymphopenia. At present, with his low white count and only 7 per cent lymphocytes, further irradiation should be withheld unless the pain makes it very urgent. There may be a rapid decline if irradiation

tion is given when so few lymphocytes appear in the bloodstream. This is one of the atypical forms of lymphatic leukemia in which most of the pathologic change appears in the spleen and lymph-glands, and the characteristic blood-picture is not so evident as in the outspoken types of lymphatic leukemia.

Some of the features of the first case are shown in a modified form in the second case.

Case II—This man is a clerk, twenty-nine years of age. He, too, suffers from backache which has troubled him for about two years. He first realized that he tired very easily and was getting progressively weaker. A pain developed in the left side of the upper part of his abdomen, and also in the lumbar and sacral regions of his back. The pain was constant and burning in character, and did not appear to improve much under treatment. For the past year he has been having night-sweats and his sleep has been interrupted because of pain. His weight has decreased from 125 to 90 pounds, a loss of 35 pounds during the past year. He sought the advice of a physician about a year ago because of a swelling in his neck. It was found that he had enlarged cervical, axillary, and inguinal lymph-nodes, and that his spleen was easily palpable. Treatment with the Roentgen rays was given at that time with little immediate effect on the axillary and inguinal nodes. The cervical ones did not decrease, but enlarged greatly and extended up behind his ear, causing impairment of hearing. During the next three months these nodes decreased in size spontaneously.

When the patient first entered our clinic, about seven months ago, he was not only poorly developed, but emaciated and distinctly sick. His spleen and cervical, axillary, left supraclavicular, and inguinal lymph-nodes were considerably enlarged. The largest node or, rather, mass of nodes was at the angle of the left side of the jaw, and measured about 5 by 6 cm.

The blood examination showed as follows:

Red blood-cells	3,200,000 per cu. mm.
Hemoglobin	60 per cent
Leukocytes	12,000 per cu. mm.

Differential leukocyte count

	Per cent
Polymorphonuclear neutrophils	70 0
Polymorphonuclear eosinophils	1 0
Small lymphocytes	10 0
Large lymphocytes	2 0
Large mononuclears	14 0
Blood-platelets slightly increased	

The urine contained a trace of albumin, some hyaline casts, a few leukocytes, and many mucous shreds. No evidence of blood was found in the feces.

The temperature was high in the evenings, between 101° and 104° F, and 2 to 3 degrees lower in the mornings. The pulse was rapid, varying with the fever, from 90 to 140. The respirations varied from 20 to 30 per minute.

A node removed from the groin was identified by Dr J Homer Wright as showing malignant lymphoma of the type described by Dorothy Reed.

After several treatments with radium over the large lymph-nodes they were reduced markedly in size, although only temporarily. The fever varied, some weeks being high, and at other times the patient had a normal temperature for several days. This patient's backache was temporarily relieved for varying periods after irradiation.

If there had not been the enlarged peripheral lymph-nodes and spleen, the diagnosis would have been much more difficult, and the abdominal and back symptoms would have suggested various other possibilities than a form of lymphoma. There was a definite history of two attacks of gonorrheal urethritis earlier in life. A gonorrheal arthritis or a diseased prostate might have accounted for his pain. There was also a history of peridental abscesses so severe that all the teeth in the upper jaw had been extracted. This, however, was ten years ago, so that it is rather late now to attribute a chronic arthritis to this source. The enlarged lymph-nodes and spleen and the pathologic changes revealed by biopsy are the important points in making the diagnosis. Fever is a common symptom of Hodgkin's disease, and the lymphopenia with polymorphonuclear leukocy-

tosis and increase in the number of mononuclear cells and blood-platelets are characteristic of the disease when advanced

The patient now is *in extremis* and illustrates the terminal stages of Hodgkin's disease. He is markedly anemic, weak, emaciated, and appears prostrated and toxic. He sleeps or dozes most of the time, and his pain is being dulled by sedatives until he obtains his natural and imminent release from this dread condition.

Backache, as well as abdominal pain, is by no means an uncommon symptom of the conditions causing enlargement of lymph-nodes. The mechanism seems to be that of mechanical pressure on the nerves, and the quickest method of giving relief is by means of adequate irradiation directed at the proper area. Irradiation does not cure the disease, but in the majority of cases is the method of choice for giving symptomatic relief.

CLINIC OF DR. PERCY B DAVIDSON

BOSTON CITY HOSPITAL

END-RESULTS OF THE MEDICAL TREATMENT OF PEPTIC ULCER

THERE is probably no subject engaging the attention of the physician and surgeon that is enmeshed in such divergent views as the treatment of peptic ulcer of the stomach and duodenum. Until comparatively recently there were two rather distinct camps—the one advocating medical treatment, and the other surgical intervention without reference to the individual case. Such intense intolerance must, indeed, be associated with a rather fundamental lack of realization of the principles involved in the opposing therapy and vagueness in the definition of the term “cure.” Most of our data on the efficacy of any form of treatment is based on immediate results rather than the ultimate efficacy. It is hoped that the demonstration of the following 2 cases will emphasize what may be expected from carefully regulated medical treatment in certain cases of peptic ulcer.

Case I—The patient, J M S, factory superintendent, referred to Dr C R Ohler by his family physician, entered the fourth medical service of the Boston City Hospital on April 16, 1923 with the following complaints: “Gnawing pains in the stomach two and a half hours after meals. Nervousness. Run down. Chronic catarrh. Vomiting. Constipation.” His family history was negative except for tuberculosis in one brother. His past history showed the presence of many childhood infections, an appendectomy in 1916, hemorrhoids for the past five years, with occasional bleeding, occasional frontal headaches, and the extraction of all his teeth several years ago because of

decay He has worn glasses for reading for the past ten years Moderate use of alcohol and tobacco has been the case since youth His occupation for the past twenty years has been that of superintendent in a suspender factory

He dates the onset of his present illness to two years ago, when retching in the morning, gnawing pains in the epigastrium, occurring about two and a half hours after meals, and relieved by food and change in posture (to the recumbent), were features Alkalies were never tried These pains sometimes became very severe, but had no definite radiation Occasionally within an hour after meals he would vomit At no time did he have hematemesis or tarry stools Pyrosis was only an occasional symptom The symptoms were practically constantly present for the past two years, and became progressively worse, accompanied by marked "nervousness," general malaise, constipation, and loss of weight (25 pounds)

On physical examination the following prominent features were present anxious facies, marked arcus senilis, sluggish spring-like pupillary light reactions, no focal infection in mouth or sinuses, hyperresonance over entire pulmonary fields, definite epigastric tenderness on pressure, inguinal hernia easily reducible, sclerosed peripheral vessels, ordinary arterial tension, normal deep reflexes, and fibrotic external hemorrhoids

The history and physical examination suggested duodenal ulcer as the principal diagnosis, as did the Roentgen studies at the Massachusetts General Hospital done on February 2, 1923 It seemed that gall-bladder disease should be carefully excluded and that the digestive features, clinically as well as radiographically, might be due to spasm secondary to a gall-bladder lesion In addition, the supplementary diagnoses of emphysema, arteriosclerosis, inguinal hernia, and external hemorrhoids were made

Laboratory findings showed Urine negative, no leukocytosis or anemia Negative blood Wassermann reaction Blood urea within normal limits Feces negative for parasites, gross and occult blood, and undigested food particles Gastric analysis (modified Ewald meal) showed in one-half hour free HCl

40 and total acidity 80 and in one hour free HCl 45 and total acidity 90, no mucus or gross or occult blood were present

The Roentgen studies were of much interest On April 19, 1923 a Rieder carbohydrate meal consisting of 60 grams of barium and 100 grams of oatmeal pap with cream and sugar, was given at 9 A M Lunch was omitted and at 3 P M the pa-

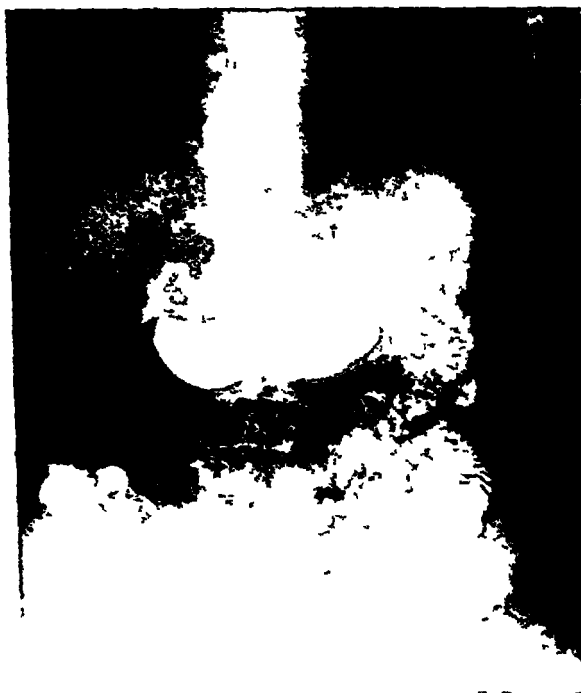


Fig 270—Case I Roentgenogram taken six hours after the ingestion of a Rieder meal before administration of atropin

tient was fluoroscoped, and showed marked gastric retention with a definite duodenal ulcer (Fig 270) A buttermilk barium mixture was now fed to study the stomach more carefully. It was hypertonic steinhorn in type, with moderate hyperperistalsis and showed no filling defects craters or incisuræ on the greater or lesser curvatures The duodenal cap filled partially, displaying a definite defect on the lesser curvature aspect of the

first portion, which could not be filled on manual palpation (Fig 271) Next day at 9 A M no gastric retention was seen, no lesions were apparent lower in the tract The diagnosis of duodenal ulcer with obstruction seemed justified It was decided, however, to x-ray the patient again under atropin to ascertain the extent of lesion due to spasm and that



Fig 271—Case I Roentgenogram taken immediately after the ingestion of a barium buttermilk mixture before the administration of atropin

due to cicatrice formation Atropin, 3/150 grain, was given between 3 P M of April 20th and 9 A M of April 21st, dilatation of the pupils did not occur, but definite dryness of the mouth was present A motor meal given at this time showed immediately a picture of the stomach similar to that seen on the previous day and a persistent duodenal deformity When viewed six hours afterward no gastric stasis was apparent (Fig 272)

A buttermilk-barium mixture still showed a persistent filling defect on the lesser curvature aspect of the first portion of the duodenum (Fig 273) Gall-bladder plates taken on April 18th showed no definite pathology in the gall-bladder region After the first examination one could conclude that we were dealing with an obstructive duodenal ulcer which warranted surgical



Fig 272 —Case I Roentgenogram taken six hours after the ingestion of a Rieder meal after the administration of atropin

treatment After the second examination, under the intensive administration of atropin, the duodenal ulcer persisted showing that a definite organic defect was present, but functionally the stomach was altered emptying in normal time this demonstrating that superimposed upon the ulcer was spasm sufficient to produce obstruction This observation led to the decision to attempt medical treatment in an endeavor to relieve the

ulcer to such an extent that the irritative features would disappear and the spasm, with the consequent gastric retention, would disappear. The patient left the hospital on April 21, 1923, to return for medical treatment.

Course in the Hospital—On May 4, 1923 the patient returned to the hospital for treatment. A modified Sippy regimen was instituted. Six ounces of milk-cream (equal parts) mixture every



Fig. 273—Case I. Roentgenogram taken immediately after the ingestion of a barium-buttermilk mixture after the administration of atropin.

hour from 7 A. M. to 7 P. M., alkaline powder starting with soda bicarbonate, 5 grains, bismuth subcarbonate, 10 grains, and calcined magnesia, 10 grains, and altered in dosage according to the degree of neutralization and frequency of bowel movements, atropin, grain 1/150, at 7 and 11 A. M. and 3 and 7 P. M. daily, and olive oil 1 ounce, at 6 30 A. M. and 9 P. M. Aspirations of gastric contents were done at frequent intervals one-half hour

after the ingestion of milk-cream mixture to determine the degree of neutralization, the contents were not aspirated nightly as in the classical Sippy treatment. After two days on such a regimen the patient became symptomless. On May 19th, after fourteen days of such treatment in bed, a Rieder carbohydrate meal was given, and fluoroscopy and the roentgenogram (Fig



Fig 274—Case I Roentgenogram showing absence of gastric stasis after fourteen days of treatment

274) showed no gastric retention. Atropin was then discontinued for two days, and roentgenograms were again taken six hours after the ingestion of a Rieder meal, showing no gastric residue. Semisolid bland food increasing gradually in amount, was now added at 8 A M noon and 5 P M feedings. He continued symptomless until May 26th when a dietary indiscretion

due to error in the diet kitchen produced gnawing pains in the epigastrium, a day's return to the milk-cream diet produced absolute relief, and the patient reached quickly his former level of tolerance for food. On June 2d, after two days of discontinuance of atropin, a motor meal was given, no gastric retention was present in six hours (Fig 275). He left the hospital



Fig 275—Case I. Roentgenogram showing absence of gastric stasis after discontinuance of atropin.

on June 2d to continue a careful regimen at home. When he left he was taking three fair-sized meals at 8 A. M., noon, and 5 P. M., with intermediate milk-cream feedings and alkaline powders. The schedule was so arranged that after two weeks at home the patient could return to work and take three moderate meals daily with three intermediate feedings of milk and cream (carried to work in a Thermos bottle), and alkalies one

hour after each ingestion of food. During his stay in the hospital, after the second day of treatment and with the exception of one day when a mistake was made in the diet, he was symptomless, he gained over 11 pounds in weight, his general condition markedly improved, particularly with regard to his psychic reactions to those about him, occult blood was persistently absent from the stools



Fig 276—Case 1 Roentgenogram showing absence of gastric stasis after four months' treatment

Course Since Leaving the Hospital—The patient remained at home on a half-rest schedule for two weeks and then returned to work, working only half a day for one month. When seen on June 15th a total gain in weight of 22 pounds was noted. He was seen on July 2d, no recurrence of symptoms had occurred, his total gain in weight was 28 pounds. He was advised to

continue on the three-meal-three-intermediate feeding basis, the variety of foods being increased. When seen again on August 15th, in the meantime writing to us every week about his condition, he was symptomless, his total gain in weight was now 30 pounds. On September 4th a rays six hours after the administration of a motor meal showed no gastric retention (Fig 276), but still a persistent deformity of the cap. He reported



Fig 277 —CASE I. Roentgenogram showing absence of gastric stasis after eighteen months' treatment.

monthly for x-ray examination and advice, but has never had a return of gastric retention or symptoms. The diet is now a very liberal one, with meat three times a week, three intermediate feedings of milk and cream are still taken daily. On November 15, 1924 the x-rays showed no gastric retention and a very marked deformity of his duodenal cap. His total gain in weight has been 37 pounds. The marked nervousness has largely

disappeared. He feels that he is cured. To us, at least, he is functioning without symptoms and Roentgen evidences of abnormal motor activity.

Inasmuch as reports have recently been published to the effect that prolonged alkalinization may be accompanied by renal damage, his renal function has been carefully followed. There



Fig 278 —Case I. Roentgenogram showing appearance of duodenal cap after eighteen months' treatment. This is not strictly comparable with Fig 271 because of differences in the position of the patient when the plate was taken.

has been a slight diminution in the ability to concentrate, but probably no more than would be expected to occur in a like period of time in a man of his age.

Case II —The patient, A. C., a widow, forty-five years of age, a domestic, was seen on February 2, 1924 because of the

following complaint "Sore stomach, especially pit, gnawing, nausea, vomiting, heartburn, flushes" Her family history was essentially negative Her husband died two years previously from pneumonia, leaving the patient without resources and necessitating her working as a domestic in addition to maintaining her home Her past history presented the following features Occasional bitemporal headache, all teeth extracted three years ago because of decay, occasional sore throats, eyes refracted for near-sightedness, slight dyspnea on moderate exertion, tendency to constipation, always "high strung," has had swollen knee one year before (probably traumatic), and supravaginal hysterectomy two months ago

She dates the onset of her present illness to twenty years ago A sharp constant pain in the epigastrium, not radiating to the back or shoulder, was the feature No relationship to meals was noted Relief was obtained by soda, heat, and, occasionally, bowel movement The symptoms were accentuated by the ingestion of food and the application of abdominal pressure Nausea and distention were occasional accompaniments of the pain Vomiting occurred seldom, but gave relief Hematemesis and melena had never occurred These symptoms of moderate severity continued practically constantly with only an occasional few days' respite until the past year, when they were markedly accentuated She had, however, not lost any weight or had any melena or hematemesis

On physical examination the following prominent findings were present Slightly overweight, rapid pulse (96), small tonsillar tags, prominence projecting anteriorly palpable in cervical region, negative heart and lungs, normal arterial tension, midline abdominal incision, abdomen generally tender, particularly in lower half and in the epigastrium

The history and physical examination suggested gastric ulcer, but because of the age of the patient cancer must be ruled out as the principal diagnosis The flushes and abdominal tenderness could all be explained on the basis of the recent hysterectomy The anterior prominence suggested a cervical rib, but was not substantiated by x-ray

Laboratory findings showed urine negative, no leukocytosis or anemia negative blood Wassermann, blood non-protein nitrogen within normal limits, feces negative for parasites, gross and occult blood, and undigested food particles. Gastric analysis (Boas meal) showed in one-half hour free HCl 5 and total acidity 11, in one hour free HCl 30 and total acidity 40, and in one and a half hours free HCl 45 and total acidity 55,



Fig 279—Case II Roentgenogram showing the crater of the gastric ulcer before treatment

50 c c of bile-stained contents were recovered from the fasting stomach, these gave a faintly positive guaiac test, but were microscopically negative

The Roentgen studies were done in the manner described for the preceding case. Six hours after the ingestion of the Rieder carbohydrate meal no gastric stasis was observed, the head of the meal was at the hepatic flexure. A buttermilk barium mixture was fed at this time to study the stomach more care-

fully It was orthotonic and did not present any abnormal motor phenomena, such as antiperistalsis or hyperperistalsis Along the lesser curvature on the posterior wall oral to the incisura angularis a large crater was noted (Fig 279) Palpation at this point elicited tenderness No hour-glass contraction was observed The duodenal cap filled readily on palpation The Roentgen diagnosis was obviously that of gastric ulcer, with the suggestion that, because of the large size, cancer be considered The clinical history (no recent loss of weight or hemorrhage) was against this, as was also the gastric analysis

The problem of therapy in this case was a real one Surgery was considered because of the possibility of its being a primary carcinoma or an ulcer which had undergone malignant degeneration, and also because of the economic status of the patient (a domestic who must do much physical work with relatively short periods of rest) On the other hand, the long-standing history, lack of recent loss of weight, and laboratory findings not confirmatory of carcinoma, as well as the patient's desire to avoid operation, suggested the advisability of a period of medical treatment, with the reservation that, should this fail to give relief, surgery be resorted to Accordingly, on February 12, 1924 the patient entered the fourth medical service for treatment

Course in the Hospital—The patient was put on a modified Sippy regimen of 3 ounces of milk and cream (equal parts) every hour from 7 A M to 7 P M, and was given magnesium oxid (usta), 10 grains, sodium bicarbonate, 5 grains, and bismuth subcarbonate, 10 grains, every hour from 7 30 A M to 9 30 P M Atropin, 1/150 grain, was given four times daily One ounce of olive oil was given at 6 30 A M and 9 30 P M The patient was symptom free on the second day of the treatment On February 22d semisolid bland food was added, increasing gradually in amount, the patient was symptom free all this time On March 11th she was put on a diet consisting of three meals and three-intermediate-feedings Her convalescence was uneventful, except for the persistence of the "hot flushes," which were apparently relieved by the subcutaneous adminis-

tration of whole ovary extract On March 20th she left the hospital on a high caloric diet in three meals and three intermediate feedings and instructions to take the alkaline powder one hour after each feeding

Course After Leaving the Hospital—Patient reported weekly and was entirely symptom free She was given subcutaneous injections of whole ovary extract weekly for two months experiencing complete relief from the "hot flushes", attempts to give ovarian and corpus luteum tablets by mouth were unsuccessful in the control of her symptoms She experienced none of her digestive symptoms at any time and returned to her usual laborious work one month after leaving the hospital She reported regularly until August 3d and then dropped out of sight On November 19, 1924 she returned stating that she has been absolutely free from symptoms and has been taking an ordinary full diet On November 20th she was x-rayed, on fluoroscopy no ulcer could be seen but on taking roentgenograms in different positions a very small crater could still be found (Figs 280, 281) She was advised to continue on a three-meal-three-intermediate-feedings basis and was told that she could not yet consider herself cured

Discussion—The 2 cases presented to you are ones which most surgeons and many physicians would, in the beginning have designated as surgical problems Yet, the results of medical treatment have been eminently satisfactory, though the institution of this therapy was rather due to the circumstances contraindicating surgery than immediate choice There are in these cases two subjects which are particularly worthy of more careful consideration and emphasis first, the criteria to be set for "cure" of peptic ulcer and, second the principles of adequate medical treatment

What constitutes cure in peptic ulcer? Is it necessarily complete anatomic restoration? Do the absence or presence of Roentgen findings in themselves without reference to the clinical picture, determine the status of an ulcer? Do the laboratory findings determine recovery? Does the absence of symptoms mean complete return to normal from the Roentgen laboratory, and anatomic standpoints



Figs 280, 281 —Case 11 Roentgenograms showing the healing of the gastric ulcer seen in Fig 279

The word "cure" in relation to peptic ulcer has unfortunately come to mean the complete restoration of normal morphology in a diseased organ. Yet even the surgeon cures fractures of the clavicle without much pretense at preserving normal morphology. Just so in peptic ulcer, situated in organs where trauma and irritation are unavoidable and scarring is an inevitable consequence of the chronic inflammatory reaction complete restoration is a goal to be sought in vain. Because of this scarring the normal physiology can hardly be expected.

The x-ray has been largely responsible for the insistence on anatomic restoration in the healing of the ulcer. One sees cases of clinical gastric or duodenal ulcer without pathology demonstrable by x-ray. On the other hand, in treated cases of gastric and duodenal ulcer who are symptom free there are usually found persistent evidences of the ulcer on x-ray. Carman, at the Mayo Clinic, feels that it is impossible to get a healed duodenal ulcer from the x-ray standpoint, provided that a previous deformity of the cap was noted. However the possibility that an erosion of the mucous membrane may be accompanied by much pathologic motor activity and give a very different x-ray picture when healed, from that when still in the abrasive fulminating state must be borne in mind. One cannot then expect the x-rays to differentiate the presence or absence of a clinical cure but can only use them as checks in the course of the disease on the extent of the lesion, and more particularly, to follow the alterations in the abnormal motor activity of the organ.

The value of gastric analysis in determining the condition of the ulcer has been greatly overemphasized. One doubts now whether there is truly an ulcer curve in gastric secretion. Possibly the presence or absence of occult blood is the only laboratory method of great consequence in determining the healing.

Our feeling is that recovery in ulcer is determined best by asymptomatic functioning. The Roentgen picture and gastric secretory curve of ulcer may persist as in Hurst's cases, but if the patient is symptomless for a sufficiently long time on a full but carefully regulated diet he may be said to be in a good

state of compensation The conditions are very similar to that of an organic heart lesion; the patient must realize that he has a physical handicap which cannot be treated specifically, and that to maintain compensation, which means to him absence of symptoms, and to the physician, abolition of such physical signs as tenderness, and more nearly normal motor activity and laboratory findings, he must adhere to certain rules of living

What are the principles of treatment which allow the patient to become and remain adequately compensated with respect to his digestive tract lesion? As the etiology of chronic peptic ulcer is a doubtful one, a specific mode of therapy is impossible The chronicity of the lesion in itself suggests that systemic as well as local factors may be influential Chronic peptic ulcer similar to the clinical condition has never been produced by any single mode of experimental procedure It appears, then, that at present one must assemble whatever experimental data seem relevant and empirical procedures which have helped clinically, and treat the patient as a whole as well as his gastric or duodenal ulcer Such treatment must be preceded by a careful history, complete physical examination, embracing all the systems as well as the digestive apparatus, and followed by laboratory and Roentgen studies of whatever nature seem indicated

The treatment may be divided conveniently into two stages first, the period of attainment of compensation, second, the period of maintained compensation Our knowledge of the pathogenesis of ulcer is so limited that, for practical purposes for the patient and the physician, the recognition of a constitutional ulcer diathesis is best It eliminates overenthusiasm on the part of either the patient or physician, and precludes careless indulgence which may precipitate loss of compensation either through a lighting up of the old ulcer or a recurrence elsewhere It is best, then, for the physician and patient to have an understanding, at the onset of the treatment, that it must be prolonged, and that constant attention to the hygiene of living must be paid to prevent recurrence of symptoms

The treatment in the attainment of compensation may be

discussed advantageously along two lines first, measures of improving general health, and, second, those directed toward healing the local lesion

A careful survey will demonstrate along what lines general treatment should proceed. The satisfactory adjustment of emotional difficulties cannot be ignored when one realizes the influence of our affective states on the motor and secretory activity of the alimentary tract. The removal of infected foci, though doubtful as to local election, improves the general health of the individual and may thus favorably influence healing. The attainment of adequate body weight in the undernourished doubtless influences metabolism and the healing processes. A careful social readjustment which may involve change in occupation and general habits of life may be necessary in some cases.

The measures for healing the local lesion are directed toward restoring normal motor and secretory functioning and the non-presentation of irritating substances. Atropin is of great assistance in relaxing spasm, which in itself may produce local ischemia, it is probably also of help in reducing the hyperperistalsis associated with lesions in the pyloric antrum and duodenum. A high fat milk-cream diet, with frequent small feedings, such as is used in the Sippy regimen is of value in reducing the acid secretion, and probably, by the late emptying of fats from the stomach, is influential in allaying the deep active waves of hunger contractions. While hyperacidity is not an invariable accompaniment of ulcer symptoms, and the therapeutic action of alkalis is indefinite, it is our impression that alkalinization as advocated by Sippy is desirable. All these measures are of value if used in relationship to the individual case and checked up carefully in relationship to tolerance, which is based, first, on the patient's symptoms, second, on Roentgen findings (as was done in Case I), and third, on laboratory studies, particularly those for the determination of occult blood.

A series of graded diets which are arranged to conform to the tolerance of the individual have been devised, with the aid of our dietitian, Miss McGovern. These are divided into four groups, the so-called A, B, C, and D diets. The A diets are

given over the period of hourly milk-cream feedings, the amount varying in individual cases. The *B* diets attempt to get the patient's tolerance to foods other than the hourly milk and cream which is continued. The *C* diets, with milk and cream every two hours, aim, in a preliminary manner, to get the patient on a three-meal basis. The purpose of the *D* diets, with three adequate meals and three intermediate feedings of milk and cream, is to prepare the patient for a normal economic and social existence. The diets are all of high caloric value, and when advanced, fat is the first food constituent to be increased because of its relatively less stimulating action on gastric secretion, and is followed in order by carbohydrates and proteins.

The patient leaves the hospital or, if treated at home, under very close scrutiny, on a three-meal-three-intermediate-feeding basis. The attainment of this stage is not based on the time in the treatment, but on the tolerance as evidenced by absence of symptoms, more normal motor activity, and absence of blood from the stools.

The maintenance of compensation is obtained by continuing on the three-meal-three-intermediate-feeding basis for a long time. Protein foods are advanced relatively late, red meats not being taken for six to nine months in most instances. A high caloric diet with maintenance of body weight is emphasized. Adequate rest is insisted upon, which may in certain cases alter the entire conduct of the patient's life.

After seeing such striking results as those of these 2 cases, one might question, Is surgery ever the method of choice? Perforation and uncontrollable prolonged hemorrhage are certain indications for surgery. Much obstruction due to cicatrices with a resulting atonic musculature, a condition analogous to extensive dilatation of the heart in the patient with but little cardiac reserve, cannot be eliminated unless the obstructive agent be removed surgically and adequate drainage of the organ be established. In individuals whose economic status precludes carrying out adequate medical treatment, and whose work must be laborious, the assistance of surgical intervention in addition to medical treatment must always be considered. It must be

emphasized, however, that surgery in itself probably does not remove those factors which are responsible for the initial appearance of the ulcer, and that continued medical supervision is as necessary in operated as in unoperated cases

Summary—Two cases of peptic ulcer have been presented, one in the duodenum and the other in the stomach in whom asymptomatic functioning has occurred with definite alteration in the Roentgen picture of the lesion. The criteria for "cure" of peptic ulcer, with the conclusion that at best the patient may be compensated as regards his organic lesion, are set forth. The principles of adequate medical treatment in combating the systemic and local factors are discussed. It is emphasized that surgical intervention is advisable in certain instances.

NOTE—Close co-operation with the x-ray laboratory such as has been afforded us, through the kindness of Dr P F Butler, roentgenologist to the Boston City Hospital, is necessary for the satisfactory x-ray control of treatment in ulcer cases.

CLINIC OF DR HENRY R VIETS

MASSACHUSETTS GENERAL HOSPITAL

MENINGOCOCCUS MENINGITIS

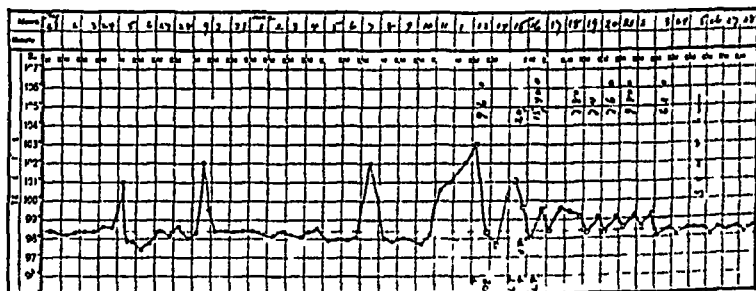
IN spite of our knowledge that meningococcus meningitis is a disease of known etiology, and that it has a specific form of treatment, both the diagnosis and the treatment are uncertain, and the disease has a mortality of 25 to 35 per cent. In other words, the pathology using the term in its broadest sense, is still poorly understood. Definite information is needed in regard to, first, the entering pathway of the organism, second the primary site of the lesion, whether it be in the blood-stream, meninges, or ventricles, third the earliest clinical manifestations, especially the intermittent type of fever, fourth the proper locus for serum treatment, whether intravenous, intraspinal, intracisternal, or intraventricular, and finally, the cause of certain postmeningitic symptoms. Some recent studies on these problems have been brought to our attention by the investigation of a single case which will serve admirably as a basis for discussion.

Case Report—A woman of twenty-nine was first seen on May 30, 1924, at the request of Dr Edward C Cook. The patient, although in bed, had few symptoms except general weakness and giddiness when she attempted to get up. Her present illness, however, had begun about four weeks before, with headache of a general character, slight purpuric rash on the extremities, joint pains, and fever. These symptoms were for the most part vague and fleeting, lasting only a few days. Three weeks later she entered a hospital at the request of her physician because of increasing attacks of headache associated with nausea. During the week prior to May 30th she had had two severe attacks of headache, mainly occipital both requiring morphin,

associated with rise of temperature to 101° and 102° F, respectively (Chart I) The attacks lasted less than twenty-four hours and each was followed by periods of no discomfort except for dizziness when the patient stood up The interval between the initial symptoms and the first attack was about three weeks, between the two attacks, four days

The past history was unimportant She had had no serious illness Glasses had been worn for over twenty years for astigmatism She occasionally had "bilious spells" Her mother

CHART I



L P Lumbar puncture
Op Operation
V P Ventricular puncture

Serum given

June 15th, Intraventricular, 60 c c
 Intraspinal, 30 c c
June 16th, Intraspinal, 35 c c

had died of pulmonary tuberculosis twenty-three years before, the patient, however, not being with her mother for the last two years of her mother's illness The patient had one normal child four years old

The first examination was of little help in making the diagnosis The patient, bright and cheerful, had no complaints when in bed She said her headache the day before had been very severe, with marked nausea The cranial nerves were normal except that both optic disks were filled and the edges blurred The rest of the neurologic examination was negative It was

noted that the equal deep reflexes were rather more easily elicited than normal. She was unsteady but the Romberg test was negative. A diagnosis of encephalitis was made at this time.

The patient was again seen nine days later (June 8th) after a third attack of headache and fever. During the interval the temperature had been normal until the day before (see Chart I) and there had been no headache. At this time the fundi showed a more definite choking. The arm reflexes were pathologically increased, and the right knee-jerk and ankle-jerk was greater than the left both being definitely increased. The Oppenheim sign was obtained upon the right, but no Babinski sign. The findings suggested increased intracranial pressure, possibly due to tumor. Continued observation in the hospital was advised. Four days later the patient showed a marked increase of symptoms. The temperature arose steadily to 102° F. The neck now became stiff and a bilateral Kernig sign was elicited, headache was severe and the patient lapsed into a partial coma. She was transferred to another hospital, and at 2 A. M. the next morning (June 13th) her first spinal fluid examination was made (see Chart II).¹ No meningococci were demonstrated in a smear, although the spinal fluid was cloudy. On further examination of the patient later in the day some ataxia of the right arm was demonstrated. A diagnosis of meningeal irritation associated with increased intracranial pressure due to brain abscess was considered. It was felt that the patient possibly had a right cerebellar abscess, although no definite cause for this abscess could be made out in the sinuses or mastoid cells by x-ray.

An exploratory cerebellar operation was done by Dr. W. J. Mixer on the afternoon of June 13th. No abscess was found, but the fourth ventricle was dilated and filled with cloudy fluid. Organisms were seen in the smear from this fluid,

¹ Cerebrospinal fluid examinations by the Neuropathological Laboratory (Dr. Frank Fremont Smith).

CHART II

CEREBROSPINAL FLUID EXAMINATION

Date and time	Source	Pressure	Character	Cells	Protein	Sugar	Smear	Cultures	Serum given	Goldzel
June 17th, 2 A M	Lumbar	Initial 400 mm 5 c.c. withdrawn 150 mm 10 c.c. withdrawn 250 mm Drained to 0 mm No block	Yellowish Cloudy Clot	Many 70 to 80 per cent polys. Many R. B. C.	222 mg. per 100 c.c.	25 to 30 mg per 100 c.c.	A few weakly Gram-positive diplococci, intracellular and extracellular	Dextrose broth 48° no growth. Hydrocele agar 120° no growth. Löffler's blood-serum 48°, no growth. Spinal fluid 48°, no growth.		0001333100
June 13th 2 10 P M	Fourth vertebral	Increased ventricle dilated	Turbid Blood tinged Clot.	Many 70 to 80 per cent polys. Many R. B. C.	23 mg. per 100 c.c.	Not done		Dextrose broth 42° contamination Löffler's blood-serum 120°, no growth. Spinal fluid 42°, no growth		0013310000
June 15th 11.20 A M	Lumbar	Initial 140 mm 40 c.c. removed No block	Turbid Yellow Cloudy	1500 per c.mm 40 per cent polys. 107 R. B. C.	84 mg per 100 c.c.	Less than 10 mg per 100 c.c.	Many Gram negative bacilli-shaped diplococci in intracellular and extracellular	Hydrocele agar 24° dew-drop colonies, Gram negative diplococci. Dextrose broth 120° no growth. Löffler's blood-serum profuse growth of meningococci		0000132300
June 15th 4 10 P M	Lumbar		Turbid Yellow Clot	4600 per c.mm 80 per cent polys. 1070 R. B. C.	82 mg per 100 c.c.	Less than 10 mg. per 100 c.c.	Many Gram negative bacilli-shaped diplococci intracellular	Hydrocele agar 72° abundant growth of meningococci. (Blood-culture 72° no growth.)	35 c.c.	0000213200
June 16th 10 P M	Lateral vertebral	Increased	Turbid Blood tinged Clot	118 per c.mm 80 per cent polys. 129 R. B. C.	21 mg. per 100 c.c.	56 mg. per 100 c.c.		Hydrocele agar 72° abundant growth of meningococci. Löffler's blood-serum abundant	60 c.c.	0122100000
June 16th 10 P M	Lumbar	Initial 300 mm. Pressure reduced to 0 30 c.c. removed.	Yellowish Cloudy Clot	Many polys.			A few intracellular diplococci	Plain agar 72° no growth. Plain broth 72° no growth	25 c.c.	
June 17th	Lumbar	Initial 270 mm. 25 c.c. removed to a pressure of 10 mm	Slightly yellow Clear No clot.		57 mg. per 100 c.c.	36 mg. per 100 c.c.	Not done.	Not done	No serum	4.00 233300

¹ Wassermann reaction negative in both blood and spinal fluid

but were not thought to be definitely meningococcic by the bacteriologic department. No growth was obtained by culture. No growth was obtained upon the fluid taken from the lumbar region the day before. After the operation the patient's temperature dropped to normal. Two days later (June 15th) the temperature again became elevated and the patient increasingly drowsy. The white count was 20,000. Another lumbar puncture done in the morning showed a cloudy yellow fluid with many typical meningococci in the smear. The diagnosis was thus definitely made after over four weeks of uncertainty. Anti-meningococcic serum was given at once into the lateral ventricles as well as the lumbar sac, 60 c c into the former and 30 c c of serum into the lumbar region. At the end of the procedure the patient complained of severe occipital headache and became unconscious for about two to five minutes, but with good pulse and respiration. Her color remained fair. She recovered spontaneously without ill effect.

Meningococci were later demonstrated by culture in the ventricular as well as the spinal fluid. On the next day (June 16th) 35 c c of serum was given into the lumbar sac. The patient improved rapidly. The spinal fluid, examined a week later, was free from organisms. Serum rash appeared June 25th and lasted three days. She was discharged from the hospital June 29th well, except for a slight but persistent elevation of the pulse, which lasted a few weeks. Five months later she appeared perfectly well. Vision, weight, and mentality were normal.

Discussion—On retrospection, our early diagnosis was faulty. It is obvious that more attention should have been paid to the three outstanding findings, namely, first, the slight but definite choked disks, second the history of joint pains and especially the purpura, and third, the intermittent type of fever.

Choked disks, although observed in cases of encephalitis, are rare. It is now generally accepted that choked disks are indicative of an increase of intracranial pressure. Such an increase is seldom found in epidemic (lethargic) encephalitis. Cheney has recently described an encephalitis patient, how-

ever, with marked choked disks, wrongly considered as a case of brain tumor ¹

Mild fever with joint pains and purpura of gradual onset occur in about one-quarter of the cerebrospinal fever cases. This is especially true in the isolated case, as this patient proved to be. In our case the history was vague of her early illness and largely obtained from the patient. The catarrhal signs, certainly the first symptoms in epidemic cases, were missing. The British workers during the war called our attention especially to this aspect of meningitis. In one series of 170 cases the initial symptoms in each was a dry catarrhal nasopharyngitis preceding the symptoms of septicemia ²

An erythematous rash occurs in about 50 per cent of cases of meningococcus meningitis, but is an extremely variable feature. A maculopapular rash is most common. Purpuric spots, an exaggerated form of the more common petechial rash, are usually seen only in fulminating or very acute cases, and "almost invariably foreshadow a fatal result" ³. The spots have recently been carefully studied and described by Brown ⁴. He made microscopic examinations and found, besides engorgement of the capillaries with leukocytes and capillary hemorrhage, numerous intracellular and extracellular meningococci. He suggests that a microscopic examination of the skin lesions might permit an early diagnosis. Moreover, meningococci are frequently found in the blood-stream in cases showing purpura, and a blood-culture should be taken at this stage of the disease.

The most striking symptom, however, in the early stages of the case was the intermittent fever. A similar type of pyrexia has recently been well described by Dock ⁵. He reports a case with intermittent fever due to meningococcus septicemia lasting

¹ Cheney, Robert C., and Parmenter, Derric C., *Boston Med and Surg Jour*, 1924, cxc, 928

² Lundie, Thomas, Fleming, and MacLagen, *British Med Jour*, 1915, i, 836

³ Worster-Drought, C., and Kennedy, A. M., *Cerebrospinal Fever*, Black, London, 1919

⁴ Brown, C. L., *Amer Jour Dis Child*, 1924, xxvii, 598

⁵ Dock, William, *Jour Amer Med Assoc*, 1924, lxxxi, 31

seven months and ending rather abruptly in fatal meningitis. Reports were found in the literature of 68 cases of meningococcemia in which there was a febrile period of at least a week without meningeal symptoms and whose clinical course changed abruptly when meningitis supervened. A typical case of meningococcemia, according to Dock, would show "intermittent fever with a rash, joint pains, and frontal headache, but with apparently good health between chills." The diagnosis may be confused with gonococcus sepsis on account of the similarity of the organisms if successful blood-cultures are obtained. Dock says that ordinary routine blood-cultures are usually sterile, the media must be enriched in order to obtain successful cultures. He recommends ascitic broth inoculated at the bedside and immediately returned to the incubator.

That meningococcemia often precedes meningococcus meningitis is well known since it was first described by Gwyn.¹ He demonstrated on Osler's Ward at the Johns Hopkins Hospital that meningococci could be recovered and cultured from both the blood-stream and the joints of a fatal case. During the war epidemic Herrick² succeeded in culturing meningococci from the blood-stream in a very large percentage of his cases seen in the septicemic stage of the disease. It is possible, moreover, to have a true bacteriemia without infection of the meninges. The bacteriemia is usually transient, perhaps not more than a few hours, but, on the other hand, it may last for days or even months, as in Dock's patient and our patient, to be followed by an acute meningeal invasion, sometimes fulminating in character.

The observations of Wegeforth and Latham³ suggest that infection of the meninges occurs not infrequently following the release of normal spinal fluid by lumbar puncture during a septicemia. They believe that the withdrawal of spinal fluid should be seriously considered as a causative factor in the pro-

¹ Gwyn, N. B., Phila. Med. Jour., 1898, ii, 1255.

² Herrick, W., Arch. Int. Med., 1918, xxi, 541.

³ Wegeforth, Paul, and Latham, J. R., Amer. Jour. Med. Sci., 1919, clviii, 183.

duction of meningitis, and advise bacteriologic blood studies in cases where the signs of meningeal irritation are absent. In this instance it is presumed that the meningococcemia stage of the disease had passed before the spinal fluid was withdrawn. A later blood-culture was negative. In the first two weeks of the patient's illness lumbar puncture was perhaps wisely avoided because of the choked disks.

The epidemiology of cerebrospinal fever is still not well understood. In the case reported above the patient lived in a small community and had not been in contact, so far as is known, with any other case. With our knowledge, however, that a patient may carry the organisms in the blood-stream for many months without very serious symptoms, it is not improbable that contact with a meningococcus carrier took place at some time before without the patient's knowledge. The danger from carriers has been demonstrated recently in a report of 9 cases, 8 of which were fatal, by Weyrauch¹. The epidemic occurred in a home for children and had been going on for about two years, the cases only occurring in one room. It was observed that it was always the new arrivals who were attacked. There was no case of meningitis in the city itself at that time. After systematic examination of the whole personnel a meningococcus carrier was discovered who had been in the institution since 1921. The infections were definitely traced to this source.

Another point of interest is in regard to the site of the primary infection. Most authorities agree that organisms enter the body via the nasopharynx and are carried to the central nervous system by the blood-stream. Anatomically it is possible for organisms to pass directly from the nasopharynx to the meninges. This route of invasion is not now considered as the most likely one on both physiologic and clinical grounds. The period of septicemia which is of course necessary if we accept the above theory of invasion may be very short and practically unnoticeable, on the other hand, it may last for months. During this period the temperature shows a characteristic series of rises, followed by periods without temperature and

¹ Weyrauch, F., *Ztschr f Hyg u Infektionskrankh*, 1923, ci, 197

often without symptoms. It is during this period that purpura and joint symptoms are most often found. There has been much discussion recently in regard to the exact site of invasion of the central nervous system from the blood-stream. There is a good deal of evidence now that the disease may attack the ventricles through the choroid plexus rather than the meninges, and that a primary ventriculitis may be the first lesion of the central nervous system. In our case, which bears out this supposition, organisms were demonstrated definitely in the ventricles after two examinations of the spinal fluid had been made with negative results. It was felt that in this case the disease was first a septicemia, then a ventriculitis, and later infection of the meninges followed. Rolleston¹ has come to the conclusion, apparently basing his opinion largely on the evidence produced by Herrick, that, "probably cerebral infection through the choroid plexuses is the usual though not exclusive site of initial infection." It is perhaps difficult to see how organisms pass through the choroid plexus and into the ventricle. The usually efficient barrier must finally break down, although resisting for weeks or even months the organisms in the blood. In those cases in which the central nervous system is never invaded, although the meningococccemia takes place, the protection is complete.

The ventricular fluid has been examined in relatively few cases on account of the supposed difficulty of ventricular puncture. Examination in children, however, has been more common on account of the ease of obtaining it through the fontanel. An easy method of obtaining ventricular fluid in adults has been used with great success by Lewkowicz.² He reports that he has tapped over 1000 cases by the use of Goetze drill, described in 1912.³ The drill has not been used, so far as I know, in this country. It is being used, however, by Purves-Stewart in England, who, I understand, has modified the drill somewhat. His observations have not been published.

¹ Rolleston, H, *Lancet*, 1919, 1, 541

² Lewkowicz, K, *Lancet*, 1924, 11, 487

³ Goetze, Otto, *Deutsche Med. Wochen*, 1912, xxxviii, 318

The successful treatment of meningococcus meningitis depends on drainage of the ventriculo-subarachnoid space plus the bactericidal action of antimeningococcus serum. It is obviously correct to give serum intravenously in the stage of septicemia or bacteremia. In the later stages, when meningeal irritation had developed, the correct site of serum injection is not so obvious. It depends upon our point of view in regard to the primary site of invasion of the central nervous system. One would feel that the serum, because of its bactericidal action, ought to be given at the place where the organisms are found. If no organisms are found in the spinal fluid removed by lumbar puncture, as in the case reported above, one should search for the organisms elsewhere. We now have a relatively easy access to the cisterna magna. This method of approach has been fully demonstrated by Ayer,¹ who has suggested that it might be a valuable place for treatment in cases of meningitis. If organisms are not found within the cistern, one should not hesitate to do a ventricular tap in order to seek out the source of infection. This method was advocated as far back as 1908 by Cushing and Sladen.² They advise ventricular puncture even in the acute stages of the disease, and if organisms are found, serum should be given. In an old case of obstructing hydrocephalus they found viable organisms long after the spinal fluid was free from meningococci. This method of ventricular injections, however, was not readily adopted, for Robb³ found only 3 cases treated by intraventricular injection in 1917.

Serum may be safely given into the cistern or into the ventricles. The reaction in the ventricles, however, may be very disturbing, as proved to be the case when 60 c c were given to the patient described above. However, nothing more than a temporary upset occurred. The reaction may possibly be due to the cresol added to the serum as a preservative. Of the efficiency of this type of treatment there seems to be no question, in our case it appeared to be a life-saving measure. Only

¹ Ayer, J. B., *Arch. Neurol. and Psychiat.*, 1920, iv, 529.

² Cushing, H., and Sladen, F. J., *Jour. Exp. Med.*, 1908, x, 548.

³ Robb, A. G., *British Med. Jour.*, 1917, i, 478.

120 c c of serum were given in all to this patient who was desperately sick. Our feeling is that the serum given into the ventricles was by far the most important.

A case successfully treated in a similar manner has recently been described by Archard, Marchal, and Laquière¹. They consider cases resistant to treatment by the lumbar route, and insist that the cranial route must be used when spinal fluid therapy does not prove to be efficient. As an illustration they give the cerebrospinal fluid findings of 1 case. In a man, twenty-seven, they found cells and organisms in the spinal fluid early in the disease, 40 c c of serum were given intraspinally and 30 c c intravenously at once. This treatment was continued every few days, but at the end of seventeen days the patient's temperature remained elevated and cells and organisms were demonstrable in the spinal fluid. They did a left frontal ventricular puncture and found organisms in the ventricular fluid also, 40 c c. of serum were given into the ventricles and 25 c c in the lumbar region at the same time. This procedure was repeated twice, two and four days after the initial treatment. The patient made an excellent recovery. After two treatments into the ventricles no meningococcus could be demonstrated in the fluid.

Hartwich² has recently reported successful treatment in 2 cases by serum intracisternally. He considers the procedure technically easier and less distressing to the patient than lumbar puncture.

The only complication occurring in our case was serum sickness, which occurred nine days after the serum was given. This is not an unusual occurrence and was not the occasion for special apprehension. The itching of the skin was very annoying. The rash and discomfort disappeared on the third day. Rolleston³ gives an excellent review of the recent literature in a paper on "The Serum Disease." It occurs in about 70 per cent

¹ Archard, Marchal, and Laquière, Bull et Mém Soc Méd d Hôp de Par, 1924, xlviii, 63

² Hartwich, A, Munch Med Woch, 1924, lxxi, 935

³ Rolleston, J D, Med Sci, 1924, ix, 443

of cases The usual symptoms—the rash, the arthritis, and the adenitis—are of no serious consequence, although they may be very annoying A more rare condition, tachycardia, shown by our patient, may be accompanied by arrhythmia

Summary—A case of meningococcus meningitis is described in which the diagnosis was uncertain for over three weeks, the main symptoms during this period being three sharp rises in temperature, with severe headaches lasting twenty-four hours at intervals of five to eight days Between attacks the patient was practically free from symptoms In the first few days of the illness there were some purpuric spots on the extremities, pain in the joints, and mild fever Early in the course of the illness a slight but definite filling of the optic cups was noted Four days after the fourth attack of fever and headache the temperature began to rise steadily and signs of meningeal irritation were present A lumbar puncture at this time gave a cloudy fluid with a few questionable organisms seen in the smear Cultures from this fluid, however, were negative Because of the severe headache, choked disks, and increasing signs of intracranial pressure a cerebellar exploration was done in the hopes of finding a brain abscess No abscess was found, but the fourth ventricle was filled with cloudy fluid from which meningococci were demonstrated in a smear and by the cultural method The next day the lateral ventricle was tapped and meningococci were grown from the ventricular fluid Treatment was inaugurated by giving serum into the ventricles and also into the lumbar sac Another treatment of serum was given the next day in the lumbar region Rapid recovery took place Convalescence was uneventful except for slight serum sickness nine days after last treatment

It was concluded that the earliest manifestations—the rash, joint pains, purpura, and slight fever—were due to general septicemia, meningococcus in type The stage of catarrhal nasopharyngitis was not noted The rash, joint pains, and purpura disappeared within a few days The meningococcemia lasted over three weeks and gave rise to the intermittent temperature characteristic of meningococcus septicemia, as well as the

severe headache Invasion of the central nervous system presumably took place from the blood-stream through the choroid plexus into the ventricles It is possible that invasion of the ventricles may have taken place very early in the disease The choked disks an early finding speak for this In that case the severe occipital headaches may have been due to a temporary obstructive hydrocephalus, relieved when the increasing pressure was sufficient to break down the artificial barrier between the ventricular and subarachnoid spaces It would be difficult if this were true to explain the long latent periods between attacks of headache and fever

When the diagnosis of ventriculitis was established anti-meningococcus serum was, therefore correctly given into the ventricles for its bactericidal action with ventricular and spinal drainage This we believe to be the best form of treatment in cases with the above characteristics

CLINIC OF DRS HOWARD B SPRAGUE AND
PAUL D WHITE

MASSACHUSETTS GENERAL HOSPITAL

HEART-BLOCK DURING AURICULAR PAROXYSMAL
TACHYCARDIA (CLINICAL OBSERVATIONS ON THREE
CASES*)

SIMPLE auricular paroxysmal tachycardia is an abnormal rhythm of the heart characterized by sudden onset and abrupt cessation of rapid regular cardiac action. The mechanism presumably is dependent upon the sudden development of an abnormal focus of impulse formation in the auricular muscle at a variable distance from the sino-auricular node. It can be proved by electrocardiographic tracings that the electrical waves propagated from the new focus are abnormal in shape but are regular in their formation and are followed by regular responses of the ventricles. The rate of both chambers is between 100 and 200 per minute, with an average rate of 140 to 190. The duration of the paroxysm is usually short, most commonly a few hours, but it may last from a few seconds to two weeks, or even longer. The essential characteristic lies in the fact that the auricles beat regularly and rapidly at a constant rate under the control of an abnormal pacemaker, but the ventricles are able to maintain an equally rapid rate by contracting in response to all the stimuli from the auricles. In other words, there is no block between the two chambers.

The condition with which paroxysmal tachycardia is most likely to be confused is auricular flutter. The mechanism of flutter, however, is different. This rhythm is due to the development of a "circus movement" in the auricle. Lewis first des-

* From the Cardiac Clinic of the Massachusetts General Hospital

cribed this phenomenon in the mammalian heart, it consists of a circular propagation of impulses about the great veins at the base of the heart. The rotary movement is regular and occurs from 200 to 350 times a minute, the usual rate being from 260 to 320. With each revolution of the "circus movement" an impulse is sent to the A-V node and the conducting system. Due, however, to the rapidity of impulse formation in auricular flutter the conducting tissue is unable to transmit all the impulses to the ventricle and a condition of partial heart-block is developed. The commonest rhythm is that of 2:1 block, resulting in a ventricular rate of one-half the auricular. The block, however, may be variable, giving an irregular heart action, which can be confused clinically with auricular fibrillation.

The duration of auricular flutter is usually much greater than that of paroxysmal tachycardia, and, although short attacks are known, it is a condition which may last for years.

Typical cases of either of these conditions are common enough. But rarely there are found examples which show unusual mechanisms electrocardiographically and present clinical features of interest. Such cases are those described in this communication, showing heart block during auricular paroxysmal tachycardia.

The infrequency of their occurrence is indicated by the fact that only these 3 cases have been observed at the Massachusetts General Hospital in the past ten years, out of a total of 5085 cases electrocardiographed. Of the 56 cases of paroxysmal tachycardia who have had records taken during paroxysms, no others have presented at any time the peculiar mechanisms that are described in the following cases.

Case I—Patient F B P Nurse Age, forty-eight

This patient first came under observation November 20, 1914 at the Massachusetts General Hospital. For one and a half years she had been troubled by attacks of rapid heart action with some palpitation and a sensation of precordial pressure on the slightest exertion. She had one syncopal attack and at the onset of her trouble had been forced to go to bed for three

months Upon recovering from this attack she developed a dull ache in the left upper quadrant of the abdomen, which had persisted ever since In December 1913, April 1914, and September, 1914 she had had similar attacks and between attacks had been troubled by palpitation, dizziness, and intermittent heart action on exertion She did not complain of dyspnea, orthopnea, or edema

Family history at the time she was first seen was negative, but one brother died of pulmonary tuberculosis in 1924

Past history showed measles and mumps in childhood and an attack of cough, weakness, and hemoptysis eight years before

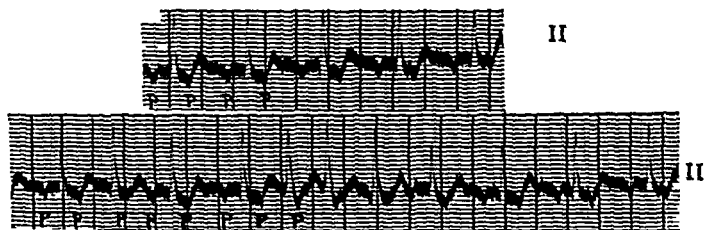


Fig 282—Case I Lead II Auricular paroxysmal tachycardia showing P waves from an abnormal focus (inverted) and ventricular arrhythmia due to varying A-V block (2 1 and 1 1) * November 23, 1914

entrance, when pulmonary tuberculosis was suspected At this time she rested for a year and had no further trouble Nine years before she had had severe tonsillitis and bronchitis There was no history of scarlet fever, diphtheria, rheumatic fever, or chorea

Physical examination showed diminished resonance at both lung apices, but no râles or abnormal breath sounds The heart apex was felt in the fifth space By percussion the borders were 3.5 cm to the right of the midsternum and 10 cm to the left The first sound was rather sharp and resembled the second sound There was one extrasystole about every thirty seconds, and a slight "presystolic" murmur at the apex The abdomen was

* In all electrocardiograms scale on abscissa = 0.2 second and scale on ordinate = 10^{-4} volt

held rather tensely and there was a tender spot below the left costal margin, but no masses or spasm were discovered

Urine, stools, and blood smear were negative Radial tracing November 21, 1914 showed occasional auricular premature beats

November 23, 1914 she had an attack of auricular tachycardia lasting about three hours and an electrocardiogram showed an auricular rate of 200 with varying degrees of A-V block (3 2, 2 1, 3 1, etc—Fig 282)

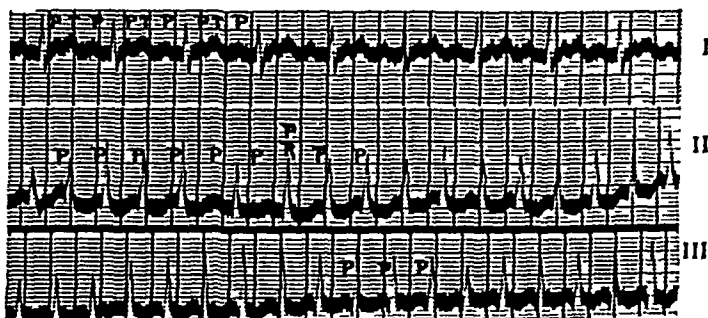


Fig 283—Case I Leads I, II, and III Auricular paroxysmal tachycardia P waves are abnormal, but from a different focus (upright) than those in Fig 282, 2 1 block in Lead I, and 1 1 rhythm in Leads II and III Auricular and ventricular arrhythmia in the first part of Lead II, with slight ventricular aberration Auricular rate, 200, ventricular rate 100 (Lead I) and 200 (Leads II and III) January 15, 1915

Rheumatic heart disease with mitral stenosis was suspected An x-ray of her chest showed some enlargement of the right side of the heart and the existence of bilateral cervical ribs She was discharged without medication December 7, 1914

January 15, 1915 she re-entered the hospital because of rapid heart action and palpitation for two days She also noted blueness of her hands Electrocardiogram showed auricular tachycardia with 2 1 block at times (Fig 283) She felt very much exhausted and her heart "pounded" hard against the chest wall This seemed more pronounced when the heart was changing from a regular rapid to a regular slow rate She was given strophanthin 1/120 grain s c, and electrocardiogram

fifteen minutes after the injection showed normal rhythm, rate 70 (Fig 284) She improved with rest and was discharged January 26 1915 She was at that time given digitalis folia $1\frac{1}{2}$ grains (0.1 gm), five times a day until saturated

August 5, 1915 she again returned, having been in bed for about a month She noticed considerable dyspnea and rapid heart action For two months she had had soreness and cracking of her finger nails and the sudden attacks of numbness, coldness, and blanching of her fingers had persisted for the previous six months A disturbance of the sympathetic system had been suggested a month before by a neurologic consultant in the Out-Patient Department

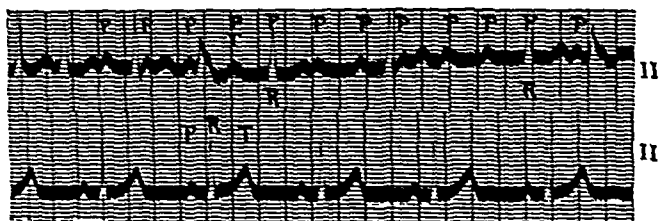


Fig 284—Case I Lead II First record shows paroxysmal auricular tachycardia with varying A-V block and ventricular aberration Second record shows normal rhythm following intravenous strophanthin, gr 1/120

Physical examination showed a slow heart with sinus arrhythmia no murmurs, but a reduplicated first sound at the apex Her hands were cold and cyanotic The skin was shriveled and dry and the finger nails marked by longitudinal ridges and occasional transverse ridges It was also discovered that the right pupil was larger than the left While in the hospital she had short attacks of auricular tachycardia She developed a respiratory infection of the influenzal type and became very sick, but her heart did not react unfavorably and she recovered and was discharged October 15, 1915 It was felt at this time that the cervical ribs might have a part in producing the cardiac irregularity, the trophic disturbances in the hands and the pupillary changes, but it was decided not to do anything about them until she recovered her strength A teleroentgenogram of

her heart August 18, 1915 showed the total transverse diameter to be 14.7 cm, right border 6.4 cm and left border 8.3 cm from the midline, length 13.8 cm, diameter of the great vessels 4.25 cm

A month later, November 13, 1915, she returned from a convalescent home, having had several slight attacks of palpitation and three attacks of cramp-like pain in her arms with contractions of the fingers. These were worse on the left than on the right. While in the hospital she had one attack in which all her fingers became dead white to the second phalangeal joint. Above this, to the middle of the palm, the hands were a deep purple color and the fingers were cold. The pallor changed to a deep cyanosis,

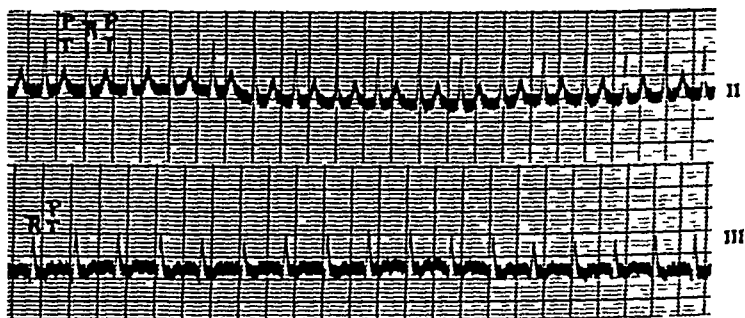


Fig. 285—Case I. Auricular paroxysmal tachycardia with 1:1 rhythm, P waves falling on T waves. Rate 190. Leads II and III. March 11, 1922.

the attack lasting in all four to five minutes. It was unassociated with cardiac irregularity except premature beats. Neurologic examination showed touch pain, and temperature sensations unaffected in the arms. Her reactions to atropin and adrenalin were tried and found to be normal.

Another x-ray of the spine showed two distinct ribs on the seventh cervical vertebrae and unusually small twelfth ribs. After considerable discussion removal of one cervical rib was decided upon.

At operation for removal of the right cervical rib it was found that the brachial trunks were lying directly on the accessory rib which, in turn, was resting on the pleura. The rib was ex-

cised The vagus and sympathetic nerves were not seen She made a good recovery and felt remarkably relieved of both cardiac and trophic disturbances She was discharged December 21, 1915

March 11, 1922 she re-entered the hospital For six years following the operation she had been considerably better The vasomotor disturbances were much improved and her attacks of palpitation had been less frequent and less severe She had been able to work almost constantly

For the three days before entrance, however, she had been having a prolonged attack of rapid heart action Electrocardio-

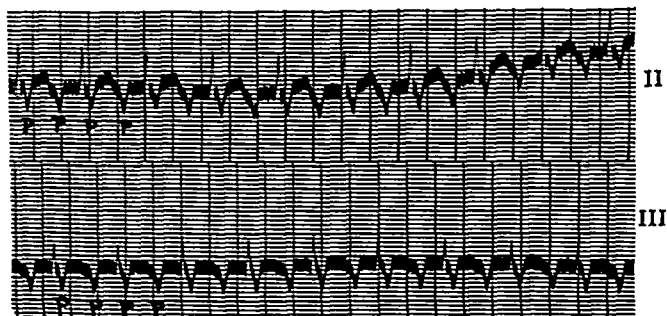


Fig 286—Case I Record taken the same day as the one in Fig 285 Leads II and III Auricular paroxysmal tachycardia arising from focus causing inverted P waves with 2:1 A-V block Auricular rate 240, ventricular rate 120 March 11, 1922

gram showed auricular paroxysmal tachycardia, rate of 190 (Fig 285) Later in the day this changed to an auricular rate of 240 and ventricular rate of 120 (Fig 286) She was digitalized and March 14, 1922 showed normal rhythm, rate of 90, and she was discharged from the hospital

September 13, 1922 she was seen again and admitted to the hospital because she had been having attacks of rapid heart action about every four days for the past six weeks At times her heart rate would remain at about 120 for a week and she would become very exhausted, although she would sometimes work during such an attack Electrocardiogram again showed

auricular tachycardia a-Ray of her heart showed a definite increase in size in all directions

Quinidin was given to her without influencing her cardiac mechanism, and she developed a skin rash from its use She was again given digitalis and discharged with normal rhythm September 30, 1922 The question of removing the left cervical rib was discussed and operation postponed, as it was felt that scar tissue on the right side might be causing the recurrence of attacks

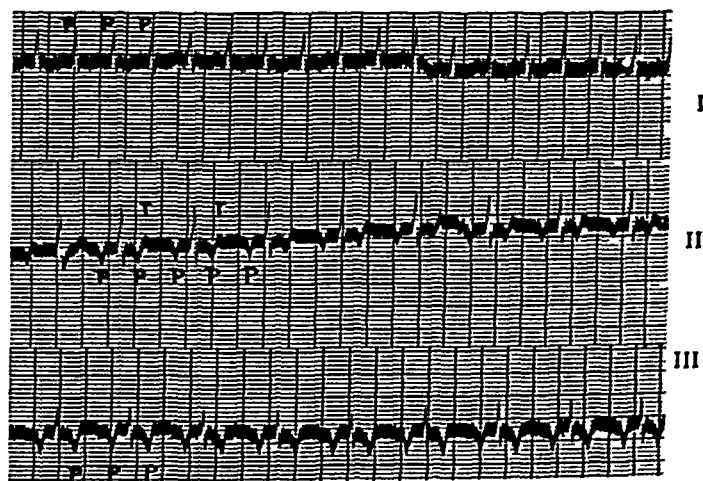


Fig 287—Case I Leads I, II, and III Auricular paroxysmal tachycardia with inverted P waves Auricular rate 210, 1:1 block in Lead I and 2:1 block in Leads II and III July 26, 1923

However, on July 26, 1923 she returned with auricular tachycardia, auricular rate 210, with varying block, 1:1 and 2:1 (Figs 287, 288) It was decided to remove the left cervical rib and after a rest period this operation was done October 16, 1923 It was followed by pain in the left arm for some time, presumably due to traction on the brachial plexus at operation Ectopic auricular tachycardia recurred after operation, but November 12, 1923 she was discharged with normal rhythm

She continued to feel very well with a few very short spells of "rapid flutter" and longer periods of "slow flutter" during

December, 1923 When seen May 27, 1924 she was working every day and had had no palpitation for a month Her heart showed normal rhythm, rate of 84, no murmurs She felt very much improved November 7, 1924 she reported only slight fluttering of her heart for about a week in August, and a few days in November, and some soreness of the fingers of both hands She was working regularly and had taken no drugs except about 15 grains of digitalis during the summer Electrocardiogram showed normal rhythm, rate of 95

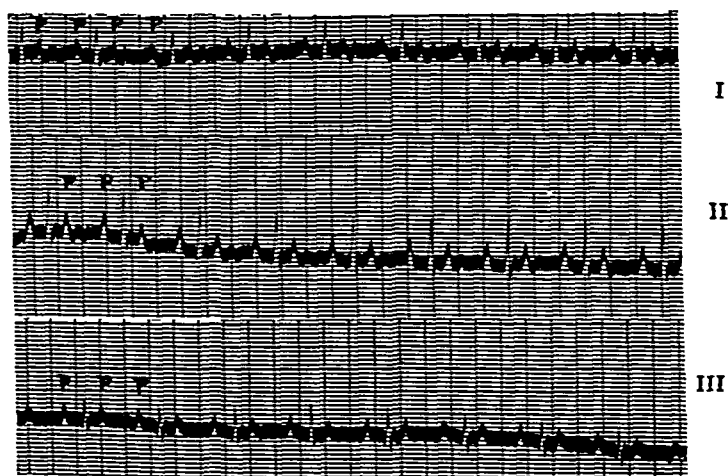


Fig 288—Case I Leads I, II, and III Record taken four days after the one in Fig 287, showing auricular paroxysmal tachycardia with upright P waves, but 2:1 block Alternate P waves fall on T waves July 30, 1922

The unusual character of this case lies in the persistence of attacks of ectopic auricular tachycardia with varying rates of auricular contraction, with and without A-V block The effect of the cervical ribs upon the cardiac mechanism is unusual and the apparent relief from excision is of interest though the relief has been by no means complete It will be seen from the electrocardiograms that this patient presents two distinct abnormal auricular foci, one giving P waves which are inverted and the other those which are upright Another point of inter-

est is illustrated in Fig. 289, in which the auricular pacemaker increased its rate, the ventricle keeping pace, up to the maximum speed of 270 beats per minute. At this rate, however, the left branch of the conducting system suddenly became unable to transmit the rapidly recurring impulses and ventricular aberration occurred because of this left bundle branch block. This ventricular rate is one of the fastest ever reported, and was previously described in a paper by one of us.¹ Finally, of much interest is the fact that greater relief is obtained by the use of digitalis in fairly large dosage at the time of the paroxysms, which are apt to last for a few days, than by any other therapeutic measure, including the administration of quinidin sulphate, to which this patient is extraordinarily sensitive.

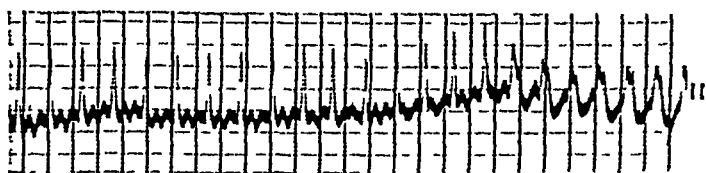


Fig. 289. Case I. Lead II. Auricular paroxysmal tachycardia with 1:1 block and increase in auricular rate to 270. The ventricle keeps pace, but at this rapid rate ventricular aberration occurs, indicating intraventricular block.

Case II - Patient L. P. Teacher of gymnastics. Age, twenty-three.

This patient was seen as a private case March 7, 1921. Her history was that for six months, following an acute gastrointestinal disturbance with diarrhea for five days, she had had attacks of tachycardia. These were of sudden onset and cessation, and lasted from two hours to five days, with an average duration of two days. She had had about twenty such attacks and was having one when she came under observation. It was associated with slight faintness and palpitation, but no pain or dyspnea. She felt perfectly well between attacks and had kept at work, but had given up vigorous exercises.

Family history was negative except that her mother had vascular hypertension.

Past History—She had had pneumonia in childhood. Tonsillectomy had been done four months before she was seen.

Physical examination was negative except for her heart. The maximal apex impulse was felt in the fifth space 8 cm to the left of the midsternum, $\frac{1}{2}$ cm within the midclavicular line. There was a reduplication of the sounds, giving a presystolic

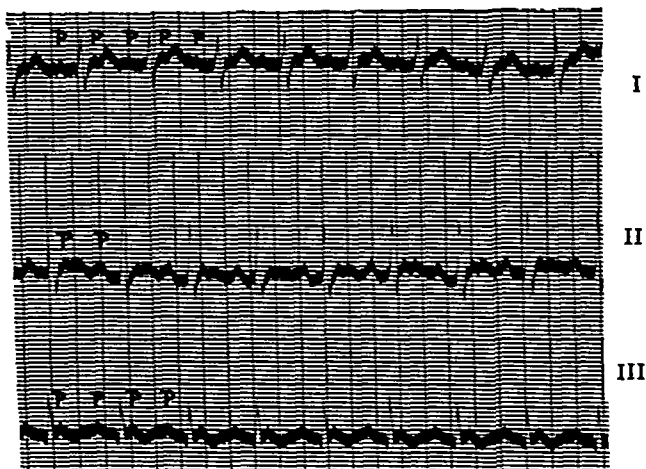


Fig 290—Case II. Leads I, II, and III. Auricular paroxysmal tachycardia with 2:1 A-V block. Auricular rate 220, ventricular rate 110.

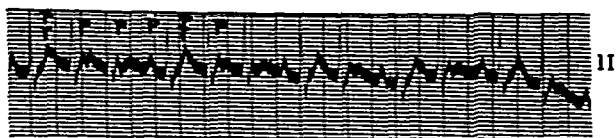


Fig 291—Case II. Lead II. After exercise, showing decrease in A-V block at times, causing ventricular arrhythmia.

gallop rhythm. The rate was 108 but at times changed to a rate twice that or to a bigeminal rate of about 150. Blood-pressure was 110 millimeters of mercury systolic and 70 diastolic. Electrocardiogram showed auricular paroxysmal tachycardia; auricular rate of 220; ventricular rate generally of 110 (2:1 block) but at times there was a variable degree of block (Fig

290). The ventricular rate was increased by exercise (Fig. 291).

She was given quinidin sulphate up to 30 grains (2 gm) a day. An attack of tachycardia occurred March 16th and lasted for three days, short attacks (twenty minutes) occurred March 23d and 25th.

Quinidin was omitted March 28, 1924, when she had normal rhythm by electrocardiogram (Fig. 292) and digitalis was advised, $1\frac{1}{2}$ grains (0.1 gm) four times a day for four or five days when the next attack occurred and $1\frac{1}{2}$ grains (0.1 gm.) once a day thereafter. An x-ray was taken which showed no evidence of



Fig. 292—Case II. Leads I, II, and III. Normal rhythm

cervical ribs. Her heart measurements were as follows: Right border 3.1 cm., left 8.1 cm., total 11.2 cm.; length 13.2 cm., base 9.4 cm.; great vessels 5.1 cm., internal chest diameter 21.2 cm.

She has been doing well on this treatment and her heart has given her very little trouble. When heard from June 7, 1924, she was continuing her work as an athletic instructor with limitation of strenuous exercise. On December 7, 1924 she reported that she had been doing very well, having had no attacks for two months. In July she had had one period of tachycardia lasting three days, in August one lasting one to two days, and in September a similar short attack. She had been able to

continue her activities during the summer and found that she could do such exercises as hiking, swimming, and dancing without difficulty. She took digitalis only during the first and last attacks, but found that rest usually was just as successful in stopping the attacks.

This case also illustrates an anomalous condition in that the electrocardiograph shows the essential mechanism to be that of paroxysmal tachycardia, there is not the even deviation of the base line characteristic of flutter, but a succession of definite upright P waves with related QRS complexes. It differs from the usual case of paroxysmal tachycardia in having an extraordinarily rapid auricular rate (220) and variable auriculoventricular block with a ventricular rate increased by exercise. It seemed that in this case digitalis was more helpful than other drugs (such as quinidin sulphate).

Case III—Patient, R. M. Italian jewelry-maker. Age, twenty-six.

This patient was first seen in the Out-Patient Department of the Massachusetts General Hospital October 15, 1914. Six months before, while playing basketball, he noticed an irregularity of his heart, which was verified by a school physician who advised limitation of exercise. He had no dyspnea, pain, cough, or edema, but was troubled much by palpitation and dizziness associated with paroxysms of rapid irregular heart beat. These paroxysms had no relation to exercise or meals and they never awakened him at night.

Family History—Negative except for insanity in one sister.

Past History—No rheumatic fever, tonsillitis, or chorea.

Physical examination was negative except for moderately enlarged ragged tonsils and the cardiac findings. His heart was forceful with a visible impulse in the third, fourth, and fifth spaces, without enlargement, rate, 64. The rhythm was irregular, with occasional premature beats and short runs of tachycardia. Rapid breathing increased the rate and the number of premature beats. Exercise did not affect the rate. The sounds were normal and there were no murmurs. A polygram four days

later showed frequent auricular premature beats, sometimes in two's and three's, and rarely in short paroxysms of tachycardia. Electrocardiograms at this time showed marked sinus arrhythmia on forced inspiration, frequent auricular premature beats arising at or near the sinus node, and short periods of auricular tachycardia.

He was given bromids and small doses of digitalis and advised to make regular visits to the clinic. Thus he has continued to do ever since and has presented essentially the same findings during the past ten years (Fig 293). He has been

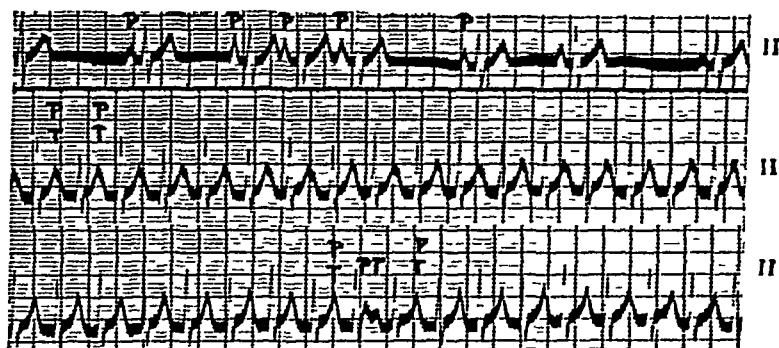


Fig 293—Case III. Lead II. Short run of auricular premature beats in first strip. Long paroxysm of auricular paroxysmal tachycardia in the second and third strips. Slight auricular arrhythmia shown best in the center of the third strip where there is one P wave falling before the T wave and a prolongation of the P-R interval.

able to work most of the time. It was felt that a slight enlargement of his thyroid gland with prominence of his eyes might mean an underlying thyrotoxicosis, but a test of his basal metabolism October, 1919 showed it to be -9 per cent. X-Ray of the heart September 29, 1919 was as follows: Heart border 3 cm. to the right of the median line and 9 cm. to the left. Total transverse diameter, 12 cm. Length of heart, 14.5 cm., base, 10.3 cm. Total transverse diameter of great vessels, 5 cm.

Medication has been with digitalis, quinidin, and bromids, from which at first there was little effect, although the results with digitalis were better than those with quinidin. The attacks

for certain periods have been of daily occurrence, but from December, 1918 to July, 1919 he was entirely free on small doses of digitalis and sodium bromid on alternate days. November 3, 1919 the effects of vagal and ocular pressure were tried. Right vagal pressure seemed sometimes to slow the pulse and to stop the paroxysms, but as the paroxysms were normally so short it was difficult to be sure.

x-Ray of the chest showed no abnormality in the thymus region and no evidence of cervical ribs.

When seen September 10, 1924 he was feeling very well, at rare intervals having short runs of rapid heart action. Electrocardiogram showed normal rhythm and a rate of 50. A few months before he was saturated with digitalis in large doses and then put on a maintenance dose of $1\frac{1}{2}$ grains (0.1 gm) a day. This

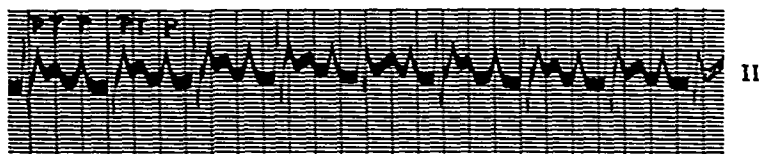


Fig 294—Case III. Lead II. Auricular paroxysmal tachycardia with 2:1 A-V block. There is slight auricular arrhythmia. Auricular rate 190.

resulted in striking relief. When he was seen November 14, 1924 his heart showed normal rhythm and he was in good health. His attacks had practically ceased and he was advised to omit digitalis in about two months.

February 5, 1925 he reported at the clinic and said that he had had no digitalis for three weeks and had noted a return of short runs of tachycardia. He was found by electrocardiograph to have a few auricular premature beats but was instructed not to take digitalis for a month more in order to see if the irregularity increased. This happened and digitalis was resumed.

The notable features in this case are (1) The great frequency over a period of ten years of auricular paroxysmal tachycardia, apparently consisting of very short runs of repeated premature beats which for months at a time were of daily and hourly occurrence sometimes permitting the heart to beat normally only a

few times a minute, (2) the occurrence of A-V and intraventricular block during a few of the paroxysms (Figs 294-296), (3) the variation in rate of these unusual paroxysms of tachycardia, which has already been noted in a previous publication by one of us², (4) the probable high auricular, and possible sino-auricular (nomotopic), site of the abnormal pacemaker, and (5) the striking relief by digitalis in large doses after all other therapeutic measures (including quinidin sulphate) had failed during this period of ten years

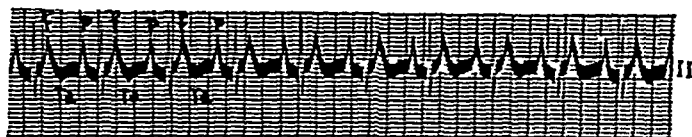


Fig 295—Case III Lead II Auricular paroxysmal tachycardia with 2:1 block (Note the well marked auricular T waves, Ta, which can be seen with the alternate P waves when they fall on the ventricular T waves *)



Fig 296—Case III Lead I Note premature auricular beat falling on the T wave of the previous ventricular complex, with prolonged P-R interval and ventricular aberration The next auricular beat is blocked

Discussion—We have presented three cases of unusual auricular paroxysmal tachycardia. The features to which we wish to call particular attention are as follows

In two of the cases the symptoms are of long duration (more than ten years). The attacks have been variable in length from those in Case III, in which the recurring paroxysms have been only a few beats long, to those of Case I whose paroxysms sometimes lasted a week.

The mechanism of especial interest is that of paroxysmal tachycardia with extraordinarily rapid and variable auricular

* See article by Sprague and White in the *Journal of Clinical Investigation*, April, 1925

rate and with varying ventricular rate due to the development of partial A-V block. Intraventricular block was also noted in two cases during periods of rapid auricular rate. The speed of the auricular contractions and the occurrence of auriculoventricular block leads to confusion with auricular flutter.



Fig. 297—Case III. Lead II. Variable A-V block, 2 1 and 3 1.

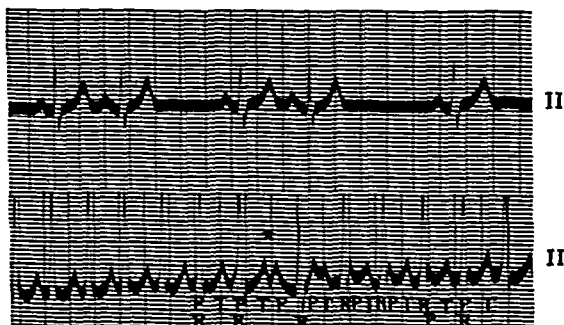


Fig. 298—Case III. Lead II. Auricular premature beats in the first record. The second strip shows one "dropped beat" at * during the course of a paroxysm of auricular tachycardia in which the P waves fall with the QRS complexes. After the blocked P wave the P-R interval is decreased from 0.27 second to 0.19 second, but gradually lengthens again to the first figure. During this transition the P waves fall between the QRS and the T waves for four cycles. The QRS wave is amplified by the coincidence of the P wave; it is observed to be more normal when it falls between the P waves immediately after the *. Some of the increase in amplitude probably results from the tachycardia.

The symptomatology of these cases tends to be similar and a certain immunity to the effects of the paroxysms seems to be developed. All of these patients have worked, often during the attacks, but have found usually that work aggravated the symptoms. They are in good health today.

In relation to treatment there is again a similarity in the resistance to quinidin therapy. No beneficial effect was secured by its use in any case. Digitalis in saturation doses acted favorably in the last case, and moderately well in the other two. The second case was helped most by rest, and the first case was apparently relieved by the removal of cervical ribs.

It is in such cases as these that the electrocardiograph is of great value, as an accurate analysis of the mechanisms involved is impossible without its assistance.

NOTE.—A recent publication by C. C. Wolfarth (*Arch. Int. Med.*, 1925, xxxv, 42) reports 2 cases with numerous fleeting paroxysms of unusual tachycardia very closely resembling the cases noted here, especially Case III. The rates of the auricular activity in these 2 cases at times were higher than those recorded in our cases, exceeding 300 per minute. It has been suggested that "intermittent auricular flutter" may be the mechanism in these cases. It did not seem likely that such a mechanism existed in the cases described by us.

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1. *Arch. Int. Med.* 1916, xviii, 712. (1 p. 5.)
2. *Arch. Int. Med.* 1920, xxx, 420.

CONTRIBUTION BY DRS ELLIOTT P JOSLIN,
HOWARD F ROOT, AND PRISCILLA WHITE

FROM THE NEW ENGLAND DEACONESS HOSPITAL

DIABETIC COMA AND ITS TREATMENT

CONTENTS

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Coma Once Not Necessarily Twice	Abdomen
The Rescued Coma Case Lives Long and Comfortably	The Kidneys in Coma
Coma Frequent Among the Poor, Rare Among the Rich	The Blood in Coma
The Changing Age Incidence of Diabetic Coma	Sugar
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Duration of Diabetes Prior to Coma	Discrepancies Between Clinical and Chemical Data
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Coma Needless	Non protein Nitrogen
The Prodromal Stage	Urinary Nitrogen
Symptomatology of Coma	Metabolism in Coma
Coma	Diagnosis
Air Hunger	Doctors' Emergency Insulin Treatment
Vomiting and Gastric Hemorrhage	Insulin Dosage
Lavage of the Stomach and its Advantages	Accessory Measures in Treatment
Exhaustion of the Coma Patient	Observations Desirable in Coma
Length of Coma Not a Measure of Severity	Rules for Treatment of Diabetic Coma in Force at the New England Deaconess Hospital, April, 1925

Introduction—In 1916 alkalis were discarded in the treatment of coma at the New England Deaconess Hospital on clinical grounds, and now after eight years comes chemical confirmation of our stand from Haldane¹ in Cambridge, England. During diabetic coma improvement is seen first clinically and only later chemically. Without the laboratory modern medicine could not exist, but there is still a field for the clinician. Here follow the reports of 48 cases of diabetic coma treated without alkalis, 15 recoveries before the discovery of insulin and 31 recoveries out of 33 cases treated consecutively with insulin, observations upon the symptoms and signs of coma, which have been made and others which should be made, and a new method of dosage of insulin based upon the doctor's estimation of the probable hours of life of the patient without insulin.

Recoveries from coma are so frequent today that it is easy for the impression to spread that coma need not be regarded seriously. Such a view is false. Coma patients recover as the result of hard work by day and by night of doctors, usually young, who intelligently apply the most modern methods of medical practice. To the various summaries of recoveries from coma at other hospitals^{2, 3, 4, 5} we wish to add another, presenting the cases in two groups, each treated without alkalis and with the administration of little carbohydrate, and further to formulate anew the standing orders for the admission and treatment of cases of coma at the New England Deaconess Hospital.

The *non-insulin group* is composed of 15 cases treated without insulin. These represented the successes, not the failures, occurring during the years 1916 to 1921, and were treated with the help of Dr. Albert A. Hornor. The *insulin group* comprises 33 successive cases of coma with 2 deaths which were admitted between January 1, 1923 and April 1, 1925. In many of the latter series we had the assistance of Dr. Dwight L. Sisco.

Treatment of the Disease, Diabetes, Rather Than of the Symptom, Acidosis. **The Cases Treated Without Insulin**—The mere recital of 48 cases of diabetic coma would lose much of its significance did it not stand for a principle. In this instance the principle is the treatment of the primary disease, diabetes,

rather than its secondary symptom, coma, the result of acidosis. The terms "acid intoxication" and "acidosis" were so compelling and the chemical indications for relief appeared so plain that, following their discovery and introduction by the Naunyn School and that school's advocacy of alkalis for acidosis, so far as we are aware up to 1916 no one urged that the fundamental fault in the diabetic metabolism in coma, the non-oxidation of carbohydrate, should be attacked exclusively with the assurance that when it was relieved the symptoms of acidosis, dependent upon it, would vanish. Yet it is true Luthje⁶ had hinted at this and had said that one need not worry about acidosis when sugar was absent from the urine. At first with fear and trembling, but soon with growing confidence, coma was treated in this clinic without alkalis until the last series of 15 recoveries without alkalis included only cases whose acidosis was indicated by plasma CO_2 combining power of 18 volumes per cent or of CO_2 tension in the alveolar air of 18 mm mercury or less^{7, 8, 9} (See Table 1, page 1876)

The results recorded in Table 1 were obtained by promptly applied medical care. Rest in bed, special nursing attendance, warmth, evacuation of the bowels by enema, the introduction of liquids into the body, lavage of the stomach, cardiac stimulants, and, above all, the exclusion of alkalis, were the means at first empirically employed. Gradually the explanation of the usefulness of these measures has become more apparent.

The Cases Treated With Insulin—The discovery of insulin and its use in coma has made recovery almost sure where it was formerly doubtful, provided well-established rules are followed. An analysis of the 31 recoveries among the 33 instances of coma between January 1, 1923, and April 1, 1925, at the New England Deaconess Hospital is given in Tables 2 and 3, pp 1877, 1878.

Increasing Frequency of Coma—Nearly twice as many cases of coma came for treatment at the New England Deaconess Hospital during 1924 as in 1923. In the earlier year there were 678 total diabetic admissions, representing 612 different diabetics, and the number in coma per admissions was 11, or 1.6 per cent., and per cases was 10 likewise 1.6 per cent. In 1924 there

TABLE 1
RECOVERY FROM IMPENDING COMA WITHOUT ALKALI OR INSULIN

Case No.	Age at coma yrs	Duration of diabetes yrs	Date	Body weight (net), Lg	FeCl ₃	NH ₄ grs. (twenty-four hour amount)	Plasma CO ₂ combining power, vols. per cent	Alveolar CO ₂ mm Hg tension	Condition			
									Alive (date)	Date	Cause	Time after recovery from coma
15	23 0	3 0	Apr 15, 1917	51 1	+	1 6	—	18		Nov 1 1917	?	7 mos
706	41 0	2 7	June 11, 1916	49 1	++	3 9	—	18		Mar 31 1917	Cardiac Coma	9 mos
918	4 5	2 2	Nov 2, 1917	10 9	++	1 3	—	18		Dec 24 1917	Coma	51 days
917	31 4	1 9	July 12, 1916	39 5	++	4 4	20 3	17 1		Nov 5 1916	Myocarditis Coma	4 mos
1011	24 5	3 3	Sept 25, 1917	31 0	++	4 4	—	15, 15, 16		Oct 1 1918		1 yr 1 mo
1012	15 7	2 7	Sept 26 1917	31 0	++	—	—	18		Jan. 22, 1919	?	1 yr 4 mos
1120	7 1	0 9	Sept 14 1917	25 9	++	2 5	30	14 15		Nov 26 1916	Coma	80 days
1106	35 1	0 8	Dec 10 1916	47 3	++	3 3	—	18		Jan 2 1918	Angina pectoris Coma	1 yr 21 days
1 00	11 5	0 6	May 29 1917	28 6	++	2 3	—	18 18		Oct 21 1917	Coma	4 mos
1110	17 9	0 8	Oct 21 1917	45 4	++	—	—	16 16		May 13 1918	Coma	7 mos
1566	45 9	6 0	Oct 21 1917	45 0	++	—	—	16 17 16		Feb 1 1921	Coma	1 yr 7 mos
			June 30 1919	43 1	++	—	18	15		May 2 1922	Empyema	1 yr, 7 mos
			July 2 1919	—	++	3 4	33	21				
			Sept 7, 1920	32 9	++	3 1	26	18				
1673	13 6	0 9	Sept 24 1920	28 8	++	3 05	—	18				
			Sept 30 1920	—	++	5 5	—	14				
			Oct 1 1920	—	++	—	27	—				
			Oct 5 1920	—	++	7 2	—	—				
			Oct 9 1920	—	++	—	—	16				
	11 3	0 9	Oct 16 1921	38 1	++	—	—	18				
1115	21 4	1 1	June 13 1922	48 9	++	—	23	18		May 1 1922	?	5 1/2 mos.
1164	15 0	0 9	Sept 20 1921	33 9	++	3 0	15 9	14 11	Apr 1925	July 7, 1922	Coma.	24 days
			Sept 10 1921	—	++	4 4	—	22 22 22				
			Oct 1 1921	—	++	—	—	26 26				
			Oct 3 1921	—	+	3 8	—	37 30				

1 On July 13 1916

¹ On July 13 1916

TABLE 2

THIRTY THREE CONSECUTIVE CASES OF COMA OR IMPENDING COMA TREATED WITHOUT AL KALI BUT WITH INSULIN

Case No	Age at coma yrs	Duration of D M, yrs	Clinical data		Blood												Urine		Insulin				
					Respiration	Mental condition	Sugar, per cent			Plasma Coa com blining power volumes, per cent			Non protein nitro- gen mgm per 100 c c			At entrance						Sugar free after entrance, hours	
							Day			Day			Day			Diabetic acid							Sugar, per cent
							1	2	3	1	2	3	1	2	3								
			1609	17 1	6 4	1923 Dec 7	Kussmaul	Drowsy	0 13	0 26	—	24	—	—	—	—	26	—	—	—	—	60	30
2118	19 3	1 3	Apr 21	Kussmaul	Drowsy	0 33	0 21	—	21	17	—	—	—	19	61	—	—	—	60	30	30		
2118	19 6	1 3	Aug 11	Kussmaul	Drowsy	0 27	0 25	—	31	13	—	—	—	37	26	—	—	—	130	50	55		
2687	25 1	1 7	Aug 28	Kussmaul	Drowsy	0 23	0 21	—	26	55	—	—	—	39	50	—	—	—	75	60	60		
2801	15 5	1 1	June 10	Kussmaul	Drowsy	0 33	0 28	0 29	16 2	13	17	—	—	—	29	30	—	—	260	30	115		
3010	22 3	1 2	Oct 21	Kussmaul	Unresponsive	0 72	—	—	12	—	—	—	—	—	47	31	—	—	80	—	—		
3010	22 3	1 6	Oct 3	Kussmaul	Drowsy	0 34	0 24	0 29	12	31	—	—	—	25	31	—	—	—	55	30	40		
3129	21 1	1 7	Dec 30	Kussmaul	Drowsy	0 37	0 28	—	22	36	—	—	—	27	—	—	—	—	90	55	55		
3129	43 2	2 1	May 13	Kussmaul	Drowsy	0 37	—	0 16	22	—	—	—	—	32	—	—	—	—	70	10	30		
3129	16 0	0 7	July 20	Kussmaul	Stuporous	0 49	—	—	13	—	—	—	—	66	36	—	—	—	60	—	—		
3182	28 4	3 1	Sept 15	Kussmaul	Unresponsive	0 55	0 17	0 30	11	71	20	—	—	—	—	—	—	—	160	90	80		
2988	56 3	1 0	Apr 21	Kussmaul	Stuporous	0 48	0 29	—	14	19	—	—	—	17	61	—	—	—	170	100	80		
3129	25 3	1 5	Oct 21	Kussmaul	Stuporous	0 16	0 27	0 36	8	19	20	—	—	19	37	—	—	—	120	35	30		
3111	17 5	1 1	Mar 29	Kussmaul	Stuporous	0 50	0 26	0 24	20	39	31	—	—	37	50	—	—	—	170	210	100		
1502	11 0	1 1	Dec 5	Kussmaul	Drowsy	0 40	0 29	—	16	39	—	—	—	39	29	—	—	—	165	25	20		
1666	29 0	0 8	May 11	Kussmaul	Drowsy	0 43	0 36	—	19	37	—	—	—	—	30	—	—	—	150	110	112		
3859	22 8	0 1	Mar 26	Kussmaul	Drowsy	0 37	0 31	0 31	25	32	30	—	—	—	31	—	—	—	100	200	175		
3477	15 3	0 7	Dec 16	Kussmaul	Drowsy	0 36	—	—	22	—	—	—	—	—	—	—	—	—	30	20	30		
1013	46 1	0 1	July 21	Kussmaul	Stuporous	0 60	0 29	0 36	21	50	—	—	—	85	61	—	—	—	210	110	80		
4109	38 8	2 6	Sept 2	Kussmaul	Stuporous	0 40	0 05	0 18	11	32	45	—	—	32	61	—	—	—	240	40	30		
1110	12 0	1 7	Sept 1	Kussmaul	Stuporous	0 16	0 19	0 31	13	30	22	—	—	22	37	—	—	—	110	20	35		
4115	51 8	0 5	Aug 21	Kussmaul	Stuporous	0 30	0 01	0 29	20	45	19	—	—	27	27	—	—	—	195	30	38		
4157	51 9	9 8	Oct 1	Kussmaul	Unresponsive	0 63	0 06	0 13	13	24	20	—	—	31	30	—	—	—	250	15	60		
1171	67 0	0 9	Sept 25	Kussmaul	Unresponsive	0 66	0 04	0 17	14	20	25	—	—	68	36	—	—	—	120	110	35		
4191	61 3	9 6	Oct 31	Kussmaul	Unresponsive	0 30	0 17	—	18	33	—	—	—	36	—	—	—	—	65	65	—		
1212	16 0	1 6	Aug 18	Kussmaul	Unresponsive	0 40	0 16	0 36	11	14	20	—	—	53	69	1	—	—	300	70	50		
1271	30 2	0 1	Dec 1	Kussmaul	Drowsy	—	0 13	—	16	35	—	—	—	22	22	—	—	—	25	100	45		
1279	61 2	2 3	Oct 28	Kussmaul	Drowsy	0 36	0 44	0 18	21	31	18	—	—	19	—	—	—	—	20	100	45		
1289	29 1	0 1	Dec 6	Kussmaul	Drowsy	0 51	0 62	0 33	11	18	32	—	—	—	—	—	—	—	115	95	45		
2021	15 3	1 3	Feb 24	Kussmaul	Emotional	0 46	—	—	16	—	—	—	—	—	—	—	—	—	65	—	50		
2786	41 5	2 7	Mar 8	Kussmaul	Unresponsive	0 59	0 36	0 29	10	21	—	—	—	43	69	—	—	—	270	80	50		
3391	17 3	2 4	Jan 9	Kussmaul	Stuporous	0 55	0 21	—	15	39	37	—	—	74	38	—	—	—	170	50	55		
3877	15 4	0 8	Mar 22	Kussmaul	Stuporous	0 77	0 15	—	16	46	—	—	—	61	18	—	—	—	270	55	40		

1 Insulin 40 units during five hours preceding blood-sugar
 2 Insulin 210 units during twelve hours preceding blood-sugar
 3 Insulin 30 units during five hours preceding blood-sugar
 4 Insulin 35 units during five hours preceding blood-sugar
 5 Insulin 60 units during eight hours preceding blood-sugar
 6 Insulin 30 units during two hours preceding blood-sugar

7 Insulin 40 units during three hours preceding blood sugar
 8 Insulin 60 units during three hours preceding blood sugar
 9 Patient given soda bicarbonate before entrance
 10 Death three and a half hours after admission
 11 Death six hours after admission

TABLE 3

CONDITION OF COMA PATIENTS TREATED WITH INSULIN AT DISCHARGE AND LATER

Case No	Entrance date	At discharge						Condition			
		Body weight (net), kg	Diet				Insulin daily units	Alive (date), 1925	Dead		
			C	P	I	Cal ories			Date	Cause	Days after recovery from coma
1923											
1609	Dec 7	42 0	33	55	110	1350	45	Apr 1	1923		
2448	Apr 24	50 7	38	43	130	1494	20	Apr 2			
2448	Aug 11	51 4	48	43	159	1795	50	Apr 2			
2687	Aug 28	57 5	38	43	127	1467	45	Apr 15			
2801	June 10	42 5	45	43	110	1342	45		Aug 18 ¹	Coma	2 mos
3021	Oct 21	59 5	—	—	—	—	—		Oct 21	Coma	
3040	Oct 3	32 7	56	51	99	1315	15	Apr 10			
3129	Dec. 30	62 0	38	51	153	1725	45	Apr 7			
3137	May 13	49 7	57	58	108	1432	16	Apr 1			
3240	July 20	—	—	—	—	—	—		July 21	Coma	
3382	Sept 15	48 3	58	58	145	1769	30	Apr 11			
1924											
2988	Apr 21	—	—	—	—	—	—		Apr 27	Pneumonia pericarditis	6 days
3129	Oct 27	61 5	45	45	157	1773	35	Apr 7			
3143	Mar 29	49 5	52	47	142	1674	28	Apr 15			
3502	Dec 5	39 3	44	54	121	1481	30	Apr 7			
3666	May 11	56 3	33	44	127	—	10	July 24			
3859	Mar 26	63 0	58	54	124	1567	13	Apr 15			
3877	Dec. 16	41 0	60	59	128	1628	35	Apr 9			
4033	July 24	79 9	63	77	136	1784	30	Apr 1			
4109	Sept 2	44 9	48	43	105	1309	15	Apr 15			
4110	Sept 1	31 7	48	46	91	1195	20	Apr 1			
4115	Aug 21	44 1	68	54	124	1601	5	Apr 3			
4157	Oct 1	—	—	—	—	—	—		Oct 10	Chronic myocarditis	8 days
4171	Sept 23	45 0	46	42	107	1315	28	Apr 7			
4194	Oct 31	—	50	30	50	770	30		Nov 8 ¹	Gangrene	7 days
4232	Aug 18	47 4	58	51	123	1543	30	Apr 1			
4271	Dec. 3	57 4	68	60	129	1673	45	Apr 1			
4279	Oct 28	41 8	76	50	99	1395	35	Apr 15			
4289	Dec 6	—	—	—	—	—	—		Dec 28	Septicemia	21 days
1925											
2024	Feb 24	—	36	44	83	1067	65	Apr 15			
2786	Mar 8	49 5	63	50	127	1595	25	Apr 7			
3391	Jan 9	42 3	63	60	129	1653	22	Apr 3			
3877	Mar 22	47 0	52	47	116	1440	45	Apr 9			
Average		49 6	52	50	120	1486	32				

¹ Not in hospital² Refused operation and left hospital against advice

were 651 total admissions, representing 505 diabetics. The number of coma cases rose to 18, or 2.8 per cent per admission, and 3.6 per cent per number of cases. In the first three months of 1925 there have been but four entries for coma. Allen and Sherrill¹⁰ predicted an increase in coma because of the increased diets due to insulin. His prediction will be fulfilled unless the

patients are diligently instructed how to avoid it. If insulin is omitted, all elements of the diet must be curtailed one-third. The converse is not so generally recognized, namely, if all food is omitted, either by design or accident, the insulin should not be given up, but reduced one-third, and it is safer then to divide each dose in halves and give twice as often. Perhaps this increase in the number of admissions for coma is due to the well warranted recognition, both on the part of the patient, his relatives, and the practitioner, that diabetic coma today is not hopeless and that unless conditions are exceptionally favorable at home it should be treated in a hospital.

Coma Once Not Necessarily Twice—The patient who was treated for coma twice in 1923 escaped it completely in 1924. Although this boy was constantly on the verge of coma in 1923, so that his parents were quite reconciled to his death, he is living happily now. One patient in coma in 1923 re-entered with it in 1924, and one in 1924 came back with the same complication in 1925, and there have been other admissions, not here recorded, in this same series for a near-coma state. Of the 33 patients treated for coma with insulin but 2 died of coma in the hospital and there has been but 1 who has died of the same complication subsequently. Two patients who recovered with us had each previously gone through coma in two other hospitals. The diabetic who knows is the diabetic who lives, provided he has the will power to do so.

The Rescued Coma Case Lives Long and Comfortably—Of the 11 admissions (10 cases) treated in 1923 there are 7 alive now. Of the 18 cases similarly treated in 1924 there are 15 alive, and all those treated in 1925 up to April 1st are living. It is not a waste of time to work over a case of coma. Note the liberal diet of these patients as displayed in Table 3 and the comparatively small dosage of insulin at discharge from the hospital. The protein, 50 grams, and carbohydrate, 52 grams, each averaged about a gram per kilogram body weight, and fat, 120 grams, was given in sufficient quantity to bring up the calories in the total diet to 30 calories per kilogram. The number of units of insulin per patient averaged 32. Oddly enough

our food values correspond almost exactly with those of Wood-yatt's¹¹ prescribed formula, $F = 2C + \frac{P}{2}$, and are well inside our own rule that if the urine of the patient remains sugar free and the protein in the diet is 1 gram per kilogram body weight, it is safe to give three times as much fat as carbohydrate. The rest of our rule is if more calories are needed, the protein can be lowered to two-thirds of 1 gram per kilogram and then the fat can be raised to four or even five times that of carbohydrate, provided the urine is kept sugar free.

Coma Frequent Among the Poor, Rare Among the Rich — Poverty and moderate means rather than wealth and a competence characterize the coma diabetic. Intelligence does not always go with wealth, but wealth provides early medical care, and that protects the rich today from coma.

The treatment of a case of diabetic coma is a luxury, to be enjoyed by the doctor at the cost of time, hours of sleep, and financial loss. In the treatment of a recent case at the New England Deaconess Hospital complicated by a carbuncle and general peritonitis, three physicians spent from two to twelve hours each at the hospital, a surgeon operated, a special nurse and three pupil nurses were almost constantly in attendance for six hours, and the laboratory work required a chemist for eight hours. Rare, indeed, is the patient with coma who can afford to make adequate compensation for his necessary treatment.

The Changing Age Incidence of Diabetic Coma —Coma is no respecter of age, but note the change in age incidence which insulin has wrought. Formerly all diabetic children died of coma, but of these 33 patients there was not one in coma under the age of ten years, yet the number of diabetic children treated by us either in hospital or home is large. In the earlier series, Table 1, 2 of the 15 cases were under ten years of age. This absence of coma in children signifies first that the education of the parents has prevented it, and second, that diabetes in children is by no means as severe as has been painted. Our first 16 children under the age of ten years to take insulin were alive April, 1925 and had then lived more than four years or nearly

three and a half times as long as 25 of our fatal diabetic children of similar age prior to Dr Allen's introduction of undernutrition in 1914. In 1923 the range in age was between ten and forty-two years but in 1924 and 1925 there were 7 coma cases of the 22 treated between forty-two and sixty-six years. The oldest patient recovered slowly, but seven months later returned for a visit in blooming health.

Influence of Weight—The weight of but 1 coma case at the time of coma exceeded 140 pounds and the weights of but 4 coma patients were as much as 130 pounds. Another patient was not weighed, but probably was in excess of 130 pounds. This low average weight represented the result of the ravages of diabetes, but the loss was not extreme, because approximately only 15, or 43 per cent. were fat at any time previously in contrast to 75 per cent. for 1000 diabetics of our series. The fat diabetic can get coma, but it takes gross mismanagement to produce it. Case No. 983 came near coma in 1916, because fasting and a low carbohydrate diet made her live on her own fat and protein, but her survival for seven years without close medical supervision and later observations proved her to be a mild diabetic when subjected to more modern treatment.¹²

Duration of Diabetes Prior to Coma—The first year of diabetes has been and still is the diabetics' danger zone, and the danger is coma. Formerly 87 per cent. of all the deaths during the first year of the disease were due to coma. In the combined groups of 48 cases here reported 17 cases had had diabetes for less than one year when the catastrophe occurred. The proportion was 1 to 3 in the insulin group of the series and 1 to 2 in the non-insulin group. On the other hand, there were 2 patients who developed coma after having survived the disease ten years. The diagnosis of diabetes was first made in 2 cases, Case No. 3859 and Case No. 4289, after coma had begun. In Case No. 3859 Dr Kilbourn, of Groton detected the diabetes and accompanying coma when first called to see the patient as she was coming down with pneumonia, and Case No. 4289 entered the hospital at midnight with thyroid toxicosis and coma, diabetes previously undiagnosed. The diagnosis of diabetes in

Case No 4276 was first made when she was in coma in another hospital. Diabetes is so frequent today that we must look for it in association with all sorts of disease and, furthermore, because the patients live so long, expect all sorts of diseases to develop during its course.

Etiology of Coma.—*Coma Needless*—Diabetic coma develops when insufficient glucose in carbohydrate, protein, and fat is oxidized to offset the simultaneous combustion of fatty acids in protein and fat. It results from overeating, is almost invariably associated with an increased metabolism, and is either of endogenous nature, as in the cases of pneumonia and thyroid toxemia just cited, or is of exogenous origin from surplus food. Overeating predisposes to diabetes, invariably makes the diabetes worse, and precipitates coma. Always the same story of overeating is found, overeating of food or body. Our pathetic histories show how necessary it still is, despite the discovery of insulin, to insist upon adherence to diabetic rules both day in and day out, and, so far as the endogenous cases are concerned, the necessity for familiarity with the use of insulin. Conversely it is becoming difficult for patients to acquire coma. Witness the gravity of the exciting cause required to induce it. On the one hand, we have severe infections—lobar pneumonia with pericarditis, bronchopneumonia, erysipelas, grippe, severe sepsis of the forearm, gangrene, hyperthyroidism—and on the other hand gross infractions of the diet, frequently combined with omission of insulin, two occurring after picnics, one following 5 quarts of milk a day in addition to other food, three in the course of treatment with Christian Science or Chiropractors. One of the latter, having given little relief with 20 spinal adjustments, was said to have promised to effect a cure by the liberation of insulin from the spine.

The Prodromal Stage—The premonitory symptoms of coma are not precise, but suggest its approach, though perhaps none are as valuable from the diagnostic standpoint as a history which discloses that the patient is running counter to fundamental laws of dietetic treatment. The onset of the coma may be sudden, though this is rare and rarer still the better the history, save in

cases taking much insulin, when it can easily supervene in a few hours and reach a high degree of severity. Nausea, vomiting, pain in the epigastrium, restlessness or languor, drowsiness and fleeting dyspnea are the common symptoms and frequently they are supplemented by pains in the head, back, and legs. The symptoms are so lacking in distinction that even the elect fail to recognize their import and attribute them to nervousness. Abdominal pains may be so severe as to simulate an attack of gall-stones, appendicitis, or perforation of a gastric ulcer. Loss of weight, loss of strength, loss of appetite, headache, constipation, in fact, anything out of the ordinary in a diabetic, is a signal to be on the watch for coma. These conditions may exist a week or more before ultimate culmination in coma.

Symptomatology of Coma—*Coma*,—Diabetic coma may pass unrecognized because the intensity of the symptoms is so variable. Even such a supposedly distinctive symptom as the coma itself may lead one astray. We have heard patients respond to questions and yet later fail to recall what had taken place with them during many hours and have no recollection of such procedures, as, for example, salt solution in amounts up to 1 liter having been subcutaneously injected on several occasions or the stomach having been washed out. There is no upper limit which the blood-sugar will reach which makes coma certain, one patient giving her name when the blood-sugar was 0.90 per cent, * and no clear low limit for the acidosis as measured by the CO_2 in the blood, since this response was elicited when the CO_2 combining power was estimated at 5 volumes per cent and for some hours did not rise to 8 and subsequently to 14 volumes per cent. As a rule coma is constant when the CO_2 is below 14 volumes per cent. One patient responded when the CO_2 was 13 volumes per cent, another at a similar level just one hour before her death, and a third when the CO_2 was 12 volumes per cent.

The duration of the coma period before treatment was actively instituted with insulin was not easily determined. So intelligent a girl as Case No. 3877 recognized the premonitory symptoms,

* Allen (verbal communication) states that dogs tolerate a blood sugar percentage of 2 per cent. readily.

called her physician, and with insulin medication, before and after her transfer to the hospital, warmth, gastric lavage, caffeine subcutaneously, and salt solution by rectum was weak, but evidently far on the road to recovery, twelve hours later Case No 3240, on the other hand, was said to have been unconscious for a day and a half prior to her admittance, yet she responded to questions between three and four and a half hours later, and her death one hour subsequently we felt due more to cardiac weakness as a result of her dilated stomach than to acid intoxication, though she counts as one of our two coma deaths After coma commenced this patient was brought by automobile one hundred miles to the hospital Case No 2801 and Case No 2687 came equal distances by train or auto and recovered, but they were given insulin at the beginning of their respective journeys

Air Hunger —The air hunger, Kussmaul's respiration, is the second most diagnostic symptom, but is likewise a variable Several years ago it was found absent in a woman, Case No 1070, when the acidosis had reached a stage 12 to 15 mm Hg in the alveolar air Root explains this disappearance of the hyperpnea in the comatose patient by the increasing exhaustion Thus in 2 cases observed before insulin the period of excitement, active Kussmaul respiration with great use of the accessory muscles of respiration, bounding rapid pulse was gradually succeeded by a period in which the rapid pulse became feebler, the respirations shallow, and the patient exhausted In this period the abolition of reflexes with incontinence of urine, divergent pupils, and other evidence of damage of the nervous system were most evident It would appear that the subsidence of the Kussmaul respiration which occurs in spite of persistent acidosis and high blood-sugar may be interpreted as a result of their toxic effect on the respiratory center, so that it no longer responds to the stimulation of low bicarbonate and non-volatile acids in the blood

Insulin seems to affect the causes of the exhaustion miraculously That the causes are not to be regarded as the high percentage of sugar in the blood or its low CO_2 content is well shown by such cases as Nos 3382, 2786, and 3129, in whom extraordinary clinical improvement occurred long before any

significant change in blood chemistry was shown. This is consistent with the view of Macleod¹³ that the seat of the activity of insulin is in the tissues rather than in the blood. Examination of the lungs with the stethoscope will sometimes disclose the imminence of the Kussmaul type of respiration when mere observation of the chest does not suggest it. Inspiration seems prolonged, of lower pitch than usual, as if the air was being drawn into a large cavity.

The air hunger cannot be as diagnostic a symptom of diabetic coma as the coma itself, but, as a matter of fact it is the more impressive feature. From experimental investigations upon animals Allen¹⁴ assigns to acetone and the lower fatty acids greater specific power in producing dyspnea and coma than to the acidosis.

Vomiting and Gastric Hemorrhage—Vomiting is recorded as having taken place in more than one-third of the cases, and it is probable that it was a precursor of the coma in nearly all. The vomiting was frequent rather than occasional in the given case, and there are several records of its having occurred daily from several days up to a week. When lavage of the stomach was promptly performed at entrance to the hospital, the effect upon the course of the coma was distinctly favorable.

The vomitus late in diabetic coma and after death the contents of the stomach frequently contain large quantities of old blood. The very presence of so much blood is proof positive of the susceptible state of the stomach in diabetic coma and emphasizes every rule given for the protection of the stomach. Formerly I (Joslin) believed that the alkalis which I had given during the treatment of the coma had much to do with this presence of blood, but now even without alkalis one sees evidence of it. The hemorrhage is not like that from an ulcer, though one does get gastric and duodenal ulcers in diabetes, but it is the hemorrhage such as one sees in various toxic conditions.

At autopsy the walls of the stomach have appeared pale and very thin. The rugæ are entirely flattened out and the lining membrane shows small petechial hemorrhages. Dr. Lawrence Smith points out that the dilatation of the organ has stretched

the stomach walls, with the result that the muscle-fibers are separated. The walls of the capillaries are so stretched that the blood probably escapes not so much by rupture of the walls as by diapedesis. This is favored by circulatory stasis.

The gastric hemorrhage in coma is also important, because it represents an additional depletion of circulating fluid. There may be an anemia during coma which the concentration of the blood may have concealed.

Evidence of hemorrhage in coma may be furnished by a leukocytosis. Often leukocytosis in coma can be explained by the presence of an infection, but this is by no means an invariable rule. The leukocytosis may in part be explained as a result of the hemorrhage itself. It is a fact that following hemorrhages a leukocytosis quickly appears, and one must ever bear this in mind when interpreting the leukocytosis of an abdominal emergency. In Case Nos 3240, 3877, 4171, 4232, and 3391 hemorrhages were especially notable. In one instance, Case No 3877, a leukocytosis of 44,000 fell over night to 13,000. On account of a few râles in the chest, suggesting a pneumonia, an injection of salt solution was not given upon entrance. Along with the fall in leukocytosis over night the pulmonary signs disappeared.

Lavage of the Stomach and its Advantages—Lavage of the stomach is advantageous in the treatment of coma for many reasons. First of all, because in this manner food which may contribute to an extension of the coma is removed, second, because the emptying of a dilated stomach gives relief to the heart, and third by removing abdominal distention it lessens the difficulty of expansion of the lungs already burdened with hyperpnœa, fourth, it removes the source of the formation of gas from fermentation which sometimes is very considerable, and fifth, it paves the way for subsequent feeding of the patient.

The danger of gastric lavage in diabetic coma is the collapse of the patient during the process. Without gastric lavage, however, the danger is still greater. The influence of a dilated stomach on the heart of a diabetic patient is as deleterious as it is in a patient after a surgical operation. Thus in our last case of coma the pulse of the patient before gastric lavage was 212,

the pulse after lavage was 160. If this patient's stomach had not been washed out, what chance would there have been for recovery? Late in coma it is true that gastric lavage is dangerous, though far more likely to save life than its omission, but the place for gastric lavage is early. It is as wrong for a physician to allow a patient with diabetic coma to die without evacuating the stomach as it is for a surgeon to allow a patient after a laparotomy to die without assuring himself that the stomach is empty. This similarity can be carried further. The diabetic patient when first seen may not have taken liquids for hours any more than the surgical patient who has had a partial gastrectomy, and so kept without food for several days, yet the stomach of each patient may be filled with gastric secretion and blood.

Experience shows its need. When one has worked for hours over a case of coma, unsuspectingly thinking the stomach to be in good condition, and then has the patient vomit food taken twelve hours or even more than a day before, he vows that he never again will neglect obtaining proof, when he is first called to the bedside, that the stomach is empty and capable of holding the liquid given.

Exhaustion of the Coma Patient—The examination of the diabetic patient in coma is not appreciated. Here is an individual who has been struggling against odds for days and perhaps for weeks or months. Sisyphus-like, he has tried in vain to replace the loss of maybe 2000 to 4000 calories in the form of sugar and β -oxybutyric acid in the urine by the ingestion of extra food, yet, unmindful of his true condition, because of his high metabolism which his food has caused, he is stimulated like the toxic thyroid case to greater and greater exertion until he finally collapses and is forced to bed not to rest, but there to be tortured with a grueling combat for breath. The food he has hitherto eaten nausea forces him to reject, the liquids he eagerly drinks he vomits. In his restlessness he throws off the clothes. Finally, beaten in his struggle for life, he falls back helpless, unconscious, with a pulse approaching 200, with a body temperature rapidly falling below normal, with so little liquid in the body that his muscles melt away before the touch, with the eyes

as soft as jellyfish, with the skin parchment dry, with the cheeks, which so recently wore the hectic flush of an increased metabolism, now showing slow recovery of the circulation to pressure, with the pulse flickering, and with the blood-pressure so low and the flow of blood so feeble that to get a specimen one may be forced to puncture the jugular, which in contrast to the other veins is large. In the brief space of hours the body has seemingly gone through months of the ravages of cancer, and death appears at hand.

Length of Coma Not a Measure of its Severity—The length of the coma is by no means a perfect measure of the severity of the coma state. In other words, the patient is not necessarily being steadily more and more poisoned from acidosis. On the contrary, it is quite possible that the acidosis is decreasing and that death ensues during recovery from the acidosis and coma, but is due to exhaustion and cardiac weakness. Coma and acidosis are not one and the same. One might almost say, the longer the patient can be kept alive in coma, the more chance of recovery, because the effect of food and other extraneous causes which brought on the coma are steadily passing off and are being replaced by undernutrition which at such a juncture is helpful. Undernutrition lowers the metabolism and thus reduces the need for combustion of glucose to offset the combustion of fat.

Anyone who takes many diabetic histories encounters now and then the story of a spontaneous recovery from diabetic coma. Those cases of coma without diacetic acid⁵ in the urine may have outlived their acidosis, though we recognize that this is not the usual and more probable explanation. What has been said is not as applicable to coma due to endogenous causes, such as exophthalmic goiter and infections, though it may hold even here. At any rate, increasing duration of the coma does *not always* signify increasing intensity of acidosis. As one cannot tell at a given moment whether the coma is increasing or decreasing, the therapeutic rule is to take the trick and begin treatment at once. Don't trust to watchful waiting with the hope the coma will become benign.

This conception of the lessening severity of coma with event-

ual recovery has seldom if ever received proper emphasis. It is of far-reaching importance in many directions. First, does it not explain in large measure why our first group of 15 cases of coma treated without insulin recovered? By good nursing care and symptomatic and expectant treatment they lived down their acidosis. Second, it is of therapeutic value: (1) because it demonstrates anew the need of early gastric lavage to remove food fuel which might be added to the acidosis flame, (2) because it renders unnecessary in many cases threateningly large single doses of insulin with the subsequent danger of hypoglycemia and indicates doses of insulin in moderate quantity at frequent—hourly or half hourly—intervals, (3) because it shows that speed in treatment must never jeopardize the patient's strength which in the last resort is all important, and (4) because it raises new hope for the diabetic patient long in coma and encourages nurses and doctors to continued hours of vigil. We do not, however, countenance the idea that all cases of coma should be treated alike and shall call attention in the discussion of insulin in coma to the demand occasionally for an initial heroic dose of insulin.

The Metabolism on the Verge of Coma—In the series of 113 diabetics whose metabolism was studied mutually by Benedict and Joslin there were 9 who died of coma and 1 of inanition within sixty days after the date of the last observation of their metabolism, and of these 2 (Case No. 1070 and Case No. 1412) died of coma in the hospital. The data obtained from these 2 patients, though incomplete, tend to show that the acidosis was decreasing rather than increasing in their last hours. The observations were all conducted in the cot chamber, and thus were made without annoyance to the patient, and because of their length are particularly accurate. The full account of these cases is published elsewhere.¹⁵

The acidosis of Case No. 1070 was severe between September 30th and October 11th, the day of her death, and although the CO_2 in the alveolar air and the excretion of ammonia in the urine did not essentially change, there was a gradual rise in respira-

TABLE 4

THE METABOLISM OF A DIABETIC (CASE NO 1070) PRECEDING COMA¹

Date	Body weight (net)	Blood sugar	Acidosis				Urinary nitrogen per twenty four hours		Diet			Carbohydrate balance	Pulse rate	Metabolism		
			Plasma CO ₂ combining power vols per cent	CO ₂ in alveolar air	Dia cetic acid	NH ₄	Total	Per kg	Carbohydrate	Protein	Fat	Cal ories		Total cal	Per kg body weight	Variation from II and B standard
	kg	per cent	m m	lit	+	gm	gm	gm	gm	gm	gm	gm		cal	cal	per cent
1917	—	—	—	17	+	2.9	7.7	0.170	17	0	0	0	—	—	—	—
Oct 1	45.1	0.31	28	13	+	3.2	7.0	0.155	25	0	0	310	101	1181	26	-6
Oct 2	45.7	0.31	28	13	+	4.8	9.6	0.210	76	0	0	420	101	1154	25	-8
Oct 3	45.1	0.40 ²	28	15	+	4.7	12.0	0.265	113	95	25	480	99	1282	28	+2
Oct 4	45.1	0.40 ²	26	14	+	4.6	11.0	0.240	96	80	25	420	99	1208	26	-4
Oct 5	45.7	0.42 ²	—	14	+	3.7	9.0	0.195	70	80	25	420	89	1101	24	-13
Oct 6	—	0.42 ²	—	12	+	3.9	5.6	0.125	56	90	25	480	—	—	—	—
Oct 7	45.0	0.32 ²	23	12	+	3.9	9.4	0.210	105	80	25	430	—	—	—	—
Oct 8	45.0	0.24	15	14	+	5.3	12.1	0.270	89	70	20	380	—	1157	27	-4
Oct 9	—	0.67 ²	19 ¹	11	—	—	—	—	89	50	30	395 ²	—	1209	26	-8
Oct 10	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 11	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 12	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 13	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 14	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 15	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 16	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 17	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 18	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 19	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 20	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 21	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 22	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 23	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 24	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 25	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 26	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 27	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 28	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 29	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 30	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Oct 31	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

¹ Full details of the metabolism of this patient before, during, and after succinylsulfonamide are given in the original publication.

² The metabolism was -23 per cent. March 18, 1917.

³ Between Oct 2 and Oct 9 1917 there were the following experiments with carbohydrate and protein diet Oct 2, 3, 4, and 5, C 17 P 5, F O Oct 2, 3, 4, and 5, C 14 P 3, F O Oct 9 C 12

to F O

⁴ In the period Oct 2 to 9 1917, the blood-sugar was not determined before breakfast as was usually done.

⁵ The diet on Oct 9 10 1917 included 8 gm. of alcohol.

⁶ The determinations in the partial volumes of urine for Oct 10 11, 1917 were as follows: diabetic acid, ++ nitrogen, 3.1 gm., NH₄ 1.3 gm., sugar 2.4 gm.

⁷ Determinations at 3.30 P M

tory quotient from first to last, indicative of a lessening of the severity of the diabetes

The metabolism of this case is actually low, but relatively high in comparison to previous observations upon her metabolism, which were -18 and -23 per cent, illustrating the treatment of diabetes by undernutrition in 1917

The metabolism of the second patient, Case No 1412, was also studied up to within two days of death. His was the more usual type of diabetic coma, because he had not been under observation. Neither the former patient nor this one was in actual coma during the tests, but they were on the verge of coma.

Case No 1412 developed diabetes in January, 1914, at the age of twenty-seven years and eleven months, and came under observation October 16, 1917. At that time he had cast aside all dietetic precautions and acknowledged eating ice-cream, sweet cakes, corn muffins, and rolls just before admittance to the hospital. This excess carbohydrate accounted for the excretion of 4200 c c of urine in the first thirteen hours following his coming to the hospital, the excretion of 210 grams of sugar, and signs of severe acidosis. On account of the acidosis fat was withdrawn from the diet and protein somewhat restricted, but carbohydrates were allowed freely. Despite these precautions the acidosis advanced and, although liquids were given freely, the bowels emptied, body heat conserved, and circulatory stimulants administered, the patient succumbed to coma on October 22, 1917. The details are given in Table 5 on p 1892.

Likewise in this patient, as actual coma drew near there was a rise in respiratory quotient, thus conforming to what we have observed in diabetic patients treated with undernutrition. On the other hand, the acidosis appeared to increase in severity, though our methods employed for its measurement were less accurate then than now.

Examination of the Patient—The examination of the patient admitted for coma must be complete, because upon it in greatest degree rests the diagnosis. Incoherent stories are usually obtained from the excited friends. Throughout the examination one should be constantly seeking for an endogenous cause of coma.

TABLE 5
THE METABOLISM OF A CASE OF SEVERE DIABETES (CASE NO 1412, MALE) ON THE VERGE OF COMA

Date	Body weight (mct)	Blood sugar	Acidosis.					Urinary nitrogen per twenty four hours		Urinary sugar per twenty four hours	Diet				Carbohydrate balance	Pulse rate	Metabolism		
			Plasma CO ₂ combining power vols per cent	CO ₂ in alveolar	Diabetic acid	NH ₃	Total	Per kg	Carbohydrate		Protein	Fat.	Calories	Variation of standard			Respiratory quotient		
1917	—	—	—	m m Hg	—	gm	gm	gm	gm	gm	gm	gm	gm	gm	gm	—	per cent	—	
Oct 16 17	46.1	0.37	—	35	++	—	—	—	—	170	—	—	—	—	1100	—	98	+28	0.71
Oct 17 17	46.1	—	39	21	++	—	—	—	—	167	210	65	0	0	940	+40	98	+33	0.72
Oct 18 17	46.2	—	—	25	++	—	17.6	0.390	—	31+	175	60	0	0	640	—	—	+33	0.76
Oct 19 20	46.3	—	—	24	++	—	6.8+	—	—	73	125	35	—	—	300	—	—	—	—
Oct 20 21	—	Death in coma	—	17	++	—	—	—	—	—	70	5	—	—	—	—	—	—	—

The examination must be repeated at frequent intervals because changes in the condition of the patient take place so rapidly. So much time is demanded for this that it is of great advantage to have assistance both for the performance of laboratory tests and also for preparing the next step in the treatment. So many doctors and nurses become absorbed in the treatment of a case of coma that records become confused, and this has led to our adoption of a coma chart with a line for each hour of the day as shown in Tables 6 and 7. There is great need for accurate records during the course of coma and much can be learned by their assembly.

Exclusion of other causes for coma, such as apoplexy, uremia, meningitis, drugs, and trauma is accomplished during the course of the examination, but certain special features should be noted.

Lungs—The presence or absence of pneumonia is important because it influences the site and amount of salt solution which one may wish to give. It is very easy to overlook pneumonia, confusing it with râles from edema or a pericarditis in the noisily breathing patients.

Pulse-rate—The pulse-rate in our series varied greatly. With Case No. 3877 before the stomach was emptied it was 212, but afterward it fell quickly to 160. Of 21 cases in which the pulse was especially observed, only in 4 was it below 100, and in half of the remainder it was between 100 and 120 and in half above 120. One can hardly relate the pulse to the basal metabolism because it was so feeble. Indeed, it would appear always desirable to combine blood-pressure estimations with the pulse-rate when endeavoring to correlate the pulse-rate and basal metabolism. The rapidity of the pulse may be out of proportion to the intensity of coma, and when its cause from a dilated stomach was found and remedied in Case No. 3877, it fell from 212 to 160 beats in a few moments. Case No. 3240 we believe died largely because the stomach was not emptied earlier. The patient is so far *in extremis* that it takes but a slight additional burden upon the heart to cause death.

Blood-pressure—The blood-pressure is a good index of the condition of the patient. Perhaps there is no better physical

TABLE 7

NAME OF PATIENT

Orders

Date

Hour

7 A. M.

N

9

10

11

12 Noon

1

2

3

4

5

6

7 P. M.

8

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sign in estimating the prognosis Case No 3382 recovered when the blood-pressure was 78/60 mm Hg, but Case No 3021 died when his blood-pressure was 70/30 In Table 6 we give a summary of the blood-pressure readings for 21 cases

TABLE 8
BLOOD-PRESSURE IN DIABETIC COMA

Fatal Case		
Case No	Blood pressure	
	Systolic	Diastolic
3021	70	30

Cases with Recovery		
2448	125	85
2687	106	74
3129	138	82
3137	124	86
3382	78	60
2988	126	70
3113	102	82
3859	108	70
4033	124	92
4109	126	80
4110	102	68
4115	154	86
4171	92	54
4194	135	65
4232	86	58
4271	126	80
4279	98	50
4289	100	0
2786	94	70
3877	102	68

The *abdomen* deserves special attention for many reasons Case No 3502 entered the hospital for coma with Kussmaul respiration and a blood CO_2 of 15.8 volumes per cent, but he

had a board-like abdomen and extreme pain without demonstrable cause as he convalesced from coma. Another patient came in partly for coma, but instead of coma had a ruptured appendix and a third under our very eyes while convalescing from severe acidosis developed an appendicitis which ruptured and caused his death. The bladder is frequently distended, even though the patient voids, and occasionally paralysis is so extreme as to simulate spinal cord disease. This happened with an old, female, diabetic derelict who had a positive Wassermann reaction, and yet she recovered. In her case there was an ascending urinary infection with a temperature of 105° F, in contrast with the patient with ruptured appendix, whose temperature scarcely arose above normal. Attention, therefore, must be paid to the kidneys, because of possible infection due perhaps to frequent catheterization. If sepsis is present elsewhere, septic kidneys may develop or, as we have noted several times in these debilitated patients, a paranephric abscess, which undetected leads to death.

A rectal temperature of 94° F, Case No 3129, and 95° F, Case No 3382, shows the extent to which the body loses heat. Case No 3021 had a rectal temperature of 94° F. (See Foster³)

The Kidneys in Coma.—The rôle of the kidneys in coma is important. They are under a peculiar strain. Their burden should not be increased by any of the measures employed in treatment. The presence of "showers of casts" in the urine is evidence of the irritation to which they are being subjected. So rarely are they absent that one is always doubtful of the diagnosis if they are not found. Albuminuria is quite as common an accompaniment and may reach as much as 2 per cent.

Anuria may develop. This occurred in Case No 1015, seen in consultation and elsewhere reported,¹⁶ who was a schoolmaster, aged forty-seven years, highest weight 206 pounds. The family and past history were negative. The onset of diabetes occurred with indefinite symptoms in February, 1916. Sugar was first discovered March 12, 1916, and three days later the urine contained 6 per cent, albumin was reported absent. The patient came under my observation for the first time on

March 18, 1916 During the preceding twenty-four hours he had been fasted except for 1 ounce of whisky in 3 ounces of black coffee, which he had taken every two hours. No other liquid had been given save about a pint of water in which a teaspoonful and a half of sodium bicarbonate had been dissolved. During this period he had vomited fluid which contained blood. He was dull, but conscious, and there was no hyperpnea. No edema. He had no fever, pulse 104, arteries not sclerotic. The systolic blood-pressure in the right arm was 66 mm. mercury, in the left arm 80 mm. mercury, and the diastolic pressure in the left arm 50 mm. mercury (Tycos apparatus). These observations were controlled by another physician. The heart was little if any enlarged and a systolic murmur was heard at the apex. The liver edge was 2 cm. below the costal margin. During the twenty-four hours 30 c.c. of urine were obtained by catheter, showing a slight trace of albumin, no diacetic acid, and a positive reaction for sugar. The sediment contained many coarsely and finely granular hyaline casts, pus, and 6 to 8 red blood-corpuscles to a field.

Death was preceded by edema of the lungs and coma, although in no wise suggesting diabetic coma. The blood-sugar taken, twelve hours before death, amounted to 1.37 per cent. The accuracy of the solutions in the test was immediately controlled with a standard solution of glucose.

Anuria with eventual recovery occurred also in Case No. 4232 who received four injections of normal saline subcutaneously. Unlike the former patient, she developed edema, a rare condition in the coma case, but here undoubtedly due to renal block as her non-protein nitrogen of 53, 69, and 139 milligrams per 100 c.c. blood on the three successive days of coma showed. This patient had been given insulin without a diabetic diet, had taken insulin irregularly, always injecting it in the same spot until an abscess formed, and following this she came to the hospital in coma.

The importance of preserving the efficiency of the kidneys in coma is shown by the large quantities of urine which were voided during coma by the exceptionable cases who recovered, as cited

in the older literature The effect of salt solution in their vulnerable state must be watched and the effect of alkalis, which stimulate the excretion of the acid bodies through the kidneys, should be recorded by those who use alkalis in the treatment of diabetic acidosis Remembrance of the young boy, Case No 4, is still vivid He temporarily recovered for a few hours from coma with the use of alkalis and excreted during three successive days of coma 437 grams of β -oxybutyric acid, as calculated from the β -oxybutyric acid and diacetic acid extracted from the urine

Already attention has been called to the dangers of catheterization of the bladder, but these should be emphasized, because at the time this is done the patients are especially feeble and their kidneys vulnerable One should get rid of an "in-dwelling" catheter as soon as possible

The urinary nitrogen and non-protein nitrogen in coma are discussed on pages 1905 and 1906

The Blood in Coma —*Blood-sugar* —The sugar in the blood in coma is high This is in contrast to the comparatively low percentage of sugar in the urine, though doubtless this too is high in the prodromal stage When the patient is overeating the excretion of sugar is large, but when nausea and vomiting set in, the sugar in the urine quickly falls, because there is comparatively little source for urinary sugar save from meager glycogen stores and katabolized body protein Any antiketogenic effect which the diabetic may derive from his carbohydrate debauch is fleeting, but the harmful ketogenic effect of his orgies in protein and fat is "oft interred with his bones" During 1923 and 1924 no case of coma showed a percentage of sugar in the blood above 0.73 per cent, but 3 recent cases have ranged between 0.59 and 0.78 per cent, and 1 case since April 1, 1925 reached 0.90 per cent Attention has been called to the patient with a blood-sugar percentage of 1.37 per cent, and Olmsted and Kahn⁴ have recorded a similar case Dehydration and nephritis apparently accounted in large measure for each of these figures The blood-sugar of our 1923 cases averaged 0.39 per cent, our 1924 cases, 0.43 per cent, and thus far in 1925 the percentage of sugar has been 0.59

per cent As insulin has often been given before the blood has been taken for a test for sugar, the percentage of sugar has undoubtedly been higher than these figures would indicate

How high the percentage of sugar in the blood can rise without the development of acidosis we do not remember to have seen stated We can say, however, that using as a measure of acidosis the ferric chlorid test we have found acidosis absent and a blood-sugar value of 1.37 per cent This was the unusual case already described when the high value for the blood-sugar was very likely in large measure due to dehydration and anuria

The height of the percentage of sugar in the blood above normal bears little relation to the consciousness of the patient The patient with the blood-sugar value of 1.37 per cent could be roused and our recent imminent coma case No. 3877, with 0.78 per cent on March 22, 1925, a higher value than observed under similar conditions in 1923 and 1924, though drowsy, was never completely unconscious, and the still more recent case, Case No. 4525, was able to give her name The high blood-sugar value of Case No. 3877 is all the more notable because the patient had already received three hours before coming to the hospital 60 units of insulin The common cause for unconsciousness in diabetic coma, therefore, must be sought elsewhere than in the percentage of sugar in the blood This much, however, can be said, we have seen no patient at the time of an attack of diabetic coma who was unconscious when the percentage of sugar in the blood was below 0.49 per cent Of course cases of hypoglycemia are excluded

The fall in the percentage of sugar in the blood from the first day to the second and third days is shown in Table 2 Although the averages are based upon values for most, they do not represent all of the cases It is remarkable that the agreement for the years is so close The fall was from 0.39 per cent on the first day to 0.24 per cent on the second day, in 1923, and from 0.43 per cent to 0.25 per cent, respectively, in 1924 On the third day in 1924 the value even rose to 0.28 per cent The 4 cases for 1925 averaged higher, 0.59 on the first day, but fell to 0.24 on the second

The blood-sugar is an easier guide for insulin medication than the CO_2 in the blood and indeed, a more rational guide. If the blood-sugar is conquered, the acidosis takes care of itself. It is the aberrant carbohydrate metabolism which is the basis for coma

*Carbon Dioxid in the Blood**—The lowest value for the plasma CO_2 combining power in volumes per cent in our cases was 8. How much lower the CO_2 can fall and yet be compatible with life we do not know. Since writing these lines we have had 1 patient with the CO_2 combining power in volumes per cent below the scale and estimated to be 5, in a few hours it rose to 8 and later to 14 volumes per cent. Olmsted has reported a value as low as 10 with recovery. The CO_2 remained under 20 volumes per cent. for five days in Case No 3129 (See Table 9). In these cases the blood-sugar had not been brought to normal, and upon studying the protocols of their treatment

TABLE 9

PERSISTENT LOW PLASMA CO_2 COMBINING POWER IN COMA WITH RECOVERY

Case No	Days				
	1	2	3	4	5
3129	8.0	18.5	19.5	13.6	18.0
4171	14.0	20.0	25.0		
4232	10.9	22.0	20.0	26.0	

it is evident too little insulin was given. During the days these patients remained with a low CO_2 value in the plasma they appeared to be in a state of exhaustion rather than suffering from acidosis *per se*. They had not regained their ability to eat. Very likely, however, the exhaustion, in reality, was a symptom of their acidosis.

The average value for the CO_2 in the plasma for 11 cases in 1923 was 21, and for 1924 was 17. Again certain of these values represent an analysis after the first dose of insulin. Upon the

* All figures for CO_2 in the blood mean the CO_2 combining power of the plasma saturated at normal alveolar tension expressed in volumes per cent.

second day of the coma period in 1923 the CO_2 had risen to 45 volumes per cent and in 1924 to 31 volumes per cent, and on the third day to 33 volumes per cent. Undoubtedly these values are low because they represent averages based upon those coma cases convalescing slowly rather than rapidly. These evidences of persisting acidosis correspond with the clinical relapses toward the coma state which patients are prone to show as a result of lack of alertness in treatment.

Discrepancies Between Clinical and Chemical Data.—The discrepancy between coma (unconsciousness), Kussmaul respiration, and the plasma CO_2 and sugar we have already recorded, but in 2 of our coma cases it especially attracted our attention. A boy, Case No. 3129, entered the hospital in a wheel chair with CO_2 in the plasma of 8 volumes per cent and yet conscious, and his improvement with a single dose of 40 units of insulin was spectacular. In Case No. 2786 the content of sugar in the blood after the patient had received 70 units of insulin was 0.59 per cent, and even after three and a half hours when 70 more units were given was essentially the same, 0.58 per cent, yet two hours before this second blood sample was taken it was perfectly evident to onlookers that the patient was clinically improving. During this interval the change in CO_2 content was from 13 volumes per cent to 15 volumes per cent. Administration of insulin was stopped not because of the slight changes in the blood, but because of the clinical improvement of the patient. As Dr. Christian remarked the next day when he happened to visit the hospital, "Here is an illustration of recovery in the ward and death in the laboratory in contrast to the more frequent experience of a clinical death and a laboratory cure." He offered the further suggestion that the condition of the blood was not an index of the condition of the tissues. This may be the correct explanation of those cases of coma who die despite the fact that the blood alkalinity has returned to normal.

Alkalis—Extraordinary Tolerance of the Body to Variations in Blood CO_2 Content.—Alkalis were given up originally by us in the treatment of acidosis because the patients vomited and the patients died. In earlier days we did not feel as free to replace

fluids by the mouth with salt solution under the skin. All concede the doses of alkalis given formerly were excessive and harmful, and, as Blum said, occasionally led to convulsions. Then, too, with the giving of alkalis more acid appeared to be liberalized. Recently Haldane, Wigglesworth, and Woodrow¹ have proved this to be the case even in a normal subject, and have gone so far as to conclude that the administration of alkalis interfered also with the combustion of carbohydrate. Their article deserves careful perusal. The decrease in the formation of ammonia, the body's means to combat acidosis, was less than one would expect after alkaline medication. Again alkalis were given up, because although the acidosis of the patient was relieved and the normal alkalinity of the blood restored, the coma progressed. It has been claimed that this is no argument against the use of alkalis, because the tissues of the patient at this stage of the coma period have been so saturated with acids and so injured that their recuperation is impossible. In the following paragraph evidence is presented against this view.

The human body is tolerant to an extraordinary degree to extreme alterations in the CO_2 content of the blood. A young man, Case No. 3129, lay for five days in the hospital with the volume of CO_2 varying between 8 and 19.5, an old woman, Case No. 4171, presented no clinical symptoms to cause worry in the three days during which her CO_2 volume per cent was between 14 and 25. Case No. 3877 appeared to be clinically *in extremis*, although not quite unconscious when her CO_2 volume per cent. was as high as 22. In contrast to these examples of exposure of the body for days to severe acidosis should be mentioned the exposure to extreme acidosis for shorter periods also with recovery. Thus the CO_2 volume per cent fell to 8 in Case No. 3129. Bock and his confrères record values as low as 8.5 per cent, also with recovery, Foster, as low as 3.0, Olmsted with 1.10 volume per cent, and Allen 10.9. At the other end of the scales is Mrs. H., a non-diabetic with cirrhosis of the liver and extreme anemia following gastric hemorrhage, with an alkalosis of 91 volume per cent CO_2 , who was unconscious for four days and then became rational. These examples illustrate the body's

tolerance for acidosis for days and for extreme acidosis for hours. The patient about to be described tolerated acidosis for a year. What the blood CO_2 content was in Case No. 344 we do not know, but the severity of his acidosis, as evidenced by his daily excretion of β -oxybutyric acid and his formation of ammonia, must have been unusually high. Just what effect the alkalis which he took had upon the situation it is difficult to determine. Throughout the period he was taking 20 or more grams of sodium bicarbonate daily. Yet eventually when tuberculosis supervened and with loss of weight his diabetes grew milder, the acidosis essentially disappeared. Exposure of the tissues, therefore, for even one year to severe acidosis is insufficient to injure them so greatly as to inhibit recovery. (See Table 10.)

TABLE 10

TOLERANCE OF CASE NO. 344 FOR ACIDOSIS DURING TWELVE MONTHS

Date	β -oxybutyric acid gm	Nitrogen gm	Ammonia	
			Total gm	$\frac{\text{NH}_3\text{-N}}{\text{Total N}}$ per cent
1910				
December 7-8	42.6	15.8	5.1	26.5
1911				
January 25, 26	48.4	19.3	7.1	31.5
March 16, 17	52.7	19.5	7.1	29.9
April 26, 27	51.0	16.3	6.3	31.8
May 28, 29	49.8		6.0	
July 30, 31	36.2	14.1	5.1	29.8
August 12, 13	51.5	8.6	4.6	41.0
September 17, 18	52.0	12.6	1.5	29.1
November 12, 13	52.0	13.0	5.5	34.8
December 25, 26	54.8	14.5	6.3	35.7
1912				
March 17, 18	6.1	9.1	0.9	8.1
March 26, 27	2.6	9.9	1.3	10.8

These various instances are cited to show that the body undergoes with impunity marked changes in the blood CO_2 content in both directions, both for long and short periods, and they raise

the question as to whether in human beings these changes ever reach such a stage that in and of themselves they are the primary cause of death

From studies made long ago at the Nutrition Laboratory upon the assimilability of carbohydrate by diabetics the conclusion was reached, still earlier enunciated by von Noorden, that no case of diabetes is ever so extreme that the capacity for burning carbohydrate is totally lost. Now we are wondering whether acidosis and alkalosis ever reach such a stage in the human body as in and of themselves to cause death. Are not the deaths which we associate with these variations in blood CO_2 really due to other factors in the overwhelming majority of instances? Such factors are an intercurrent infection, a septicemia, heart failure from exhaustion, a dilated stomach, lack of body fluids

Non-protein Nitrogen—The non-protein nitrogen may be normal in coma and it may range as high as 138 grams. The protocols show 20 analyses on the first day and of these there were 11 above 40 milligrams per 100 c c, the average for the day being 46 milligrams. On the second day there were 18 analyses with only 4 above 40 milligrams and on the third day but 2 analyses were found. These were respectively 56 and 100

The highest non-protein nitrogen in the series was found in a young girl, Case No. 4232, previously described, and occurred on the third day of the coma period when almost complete suppression of urine had existed for forty-eight hours, albuminuria was 2 per cent, and the sediment filled with casts and blood. This high value for the non-protein nitrogen, 139 milligrams per 100 c c, represent therefore, a renal block. It was accompanied by marked edema. Whether this condition of renal block was due to the diabetes or was associated with the 4 liters of normal salt solution which the patient received is a matter for speculation. Case No. 3129 also developed ascites during his convalescence from coma, and he too received one liter of salt solution. The number of high values for the non-protein nitrogen simply confirm the evidence of impairment of the renal function in coma which Külz originally observed when he described the "showers

of casts " See page 1897 for comments upon the behavior of the kidneys in coma

Urinary Nitrogen—The urinary nitrogen in coma is not a guide to the protein metabolism because of the state of the kidneys. Though the impairment of renal function is not always extreme, it is undoubtedly always present to some degree. Just because the urinary nitrogen falls during coma is not necessarily a sign that protein katabolism is becoming less active. Perhaps this is one of the reasons why no clear relation could be found between the excretion of urinary nitrogen and acidosis in the studies which we carried out in association with the Nutrition Laboratory upon 113 of our diabetics between 1908 and 1917 *

A renal function test with phenolsulphonephthalein was unfortunately not made in any of the cases during coma, when this test was done a few days after recovery the results were low. Thus 8 tests made within ten days of recovery averaged 33 per cent excretion in two hours and later tests upon the same patients averaged 55 per cent. The damage to the kidneys was evidently temporary.

Edema is rare in diabetic coma, and save for the two instances above cited we recall but one other in our entire diabetic series. In fact, the sudden disappearance of an edema is a warning of impending coma. Carbohydrate storage in the body is associated with water storage and in coma little carbohydrate is to be found in the tissues. In the 2 cases there described the patients did not enter with edema, but developed it during treatment. Renal block presumably prevented the excretion of salt.

Metabolism in Coma—The metabolism in acidosis is always a ready topic for academic discussion, but practical therapeutic hints based upon the metabolism are seldom forthcoming. It is true that Shaffer has emphasized the necessity for lowering the total metabolism to combat acidosis. Our experience at the Nutrition Laboratory indicated a rising metabolism commensurate with acidosis. This was relative if the patient had been on a low diet and absolute when upon the high diets previous to the

* Joslin. Diabetic Metabolism with High and Low Diets, Carnegie Institution of Washington, 1923, Pub No 323, p 118

undernutrition treatment of 1914 During coma there is a paucity of observations upon the metabolism, but one would expect it to fall whether recovery or death ensues It falls in recovery as a sign of the removal of the cause of the coma and it should fall toward death as evidence of exhaustion It must not be allowed to fall too far The total metabolism, however, whether high or low, is important in coma, because from it can be deduced the grams of glucose which must be oxidized to offset the katabolizing fat Let us take for example a man weighing 55 kilograms (121 pounds), age twenty-two, height 176 cm (59 inches) His basal metabolism by the Harris and Benedict scale is 1555 calories If we add to this 15 per cent for restlessness in the precoma condition and another 15 per cent for the acidosis, either per se or due to the extra food recently eaten, our total metabolism becomes 2022 calories Assume the nitrogen excretion to be 12 grams Deducting from the total calories as per Shaffer's formula, $\frac{\text{Total metabolism} - (\text{urinary N in grams} \times 100)}{50}$ = G, we have $2022 - 1200 = \frac{822}{50} = 16$ grams glucose Multiplying this by 2, as Shaffer suggests for safety's sake, as every two millimols of acid may not meet their millimol of glucose, we have $16 \times 2 = 32$ grams of glucose required to be oxidized to offset the fat metabolism Since in coma the acid in the body is about 100 grams we might add 30 grams more of carbohydrate, which should be oxidized to burn the acid stored in the tissues This would make necessary, therefore, a total oxidation of about 60 grams of carbohydrate We know there is little glycogen in the liver in coma, but in the blood there is available, allowing 5 liters of blood with 0.5 per cent. of sugar, $(5000 \text{ c.c.} \times 0.50 \text{ per cent.})$ or 26 grams more or less of carbohydrate This would leave a requirement of only (62-25) 37 grams or about 1.5 grams of carbohydrate per hour in addition to that in the blood to rid the body of acidosis in twenty-four hours, even providing the sugar in the blood was not replenished The amount of acid formed depends upon the protein and fat metabolized There is obviously, therefore, little need for much additional carbohydrate food during coma, and in fact there is need for none at all until the sugar in the blood is normal The only evidence we

recall in the other direction is Macleod's experiment on depancreatized dogs, which showed that with more carbohydrate available, more glucose per unit insulin is oxidized, but in the presence of a high blood-sugar it is a question whether this rule would hold. Therefore we feel justified in giving little carbohydrate to our patients in coma.

Our knowledge of metabolism in coma must come chiefly from observations upon the respiratory metabolism, and such are few. Already we have pointed out why the urinary nitrogen is a poor index of the protein metabolism, and recent studies upon the blood fat by Dr Rabinowitz (personal communication) at the Montreal General Hospital indicate that the changes which it undergoes bear little relation to the metabolism of body fat. Dr Rabinowitz found that the blood fat of a diabetic dropped over night with insulin medication from 18.6 to 9.4 per cent. Allowing 5 liters of blood for the body, this indicated a disappearance of 450 grams of fat or, if burned, a production of some 4000 calories. The next day there was a fall of blood fat from 9.5 to 2.1 per cent, a disappearance of 350 grams, and yet calorimetric determinations during the same interval of time showed an oxidation of but 30 grams of fat. Where did the fat go? According to Professor W. R. Bloor "the observed phenomena are to be referred to changes in permeability of the tissues to fat as well as to sugar." "The hypothesis of change of permeability by insulin is more reasonable for the fat since the fat molecule compared with that of sugar is a very stable one and not likely to undergo molecular changes easily."

The low body temperature in coma is probably due to the loss of vaporized water through the lungs and consequent loss of body heat. This may be extreme. In Case No. 3382 a two-hour chart of the rectal temperatures shows the steady rise in body temperature under the influence of insulin, fluids by mouth and rectum, and heat applied to the body. Similarly a rise in blood-pressure occurs. It reminds one of the recovery of a patient from profound surgical shock, except that the skin is dry in coma and moist in shock. Foster's article has a remarkable chart illustrating this rise of temperature. See pages 1890 and

1892 for tables illustrating the metabolism just preceding coma

Diagnosis—Repeatedly diabetic patients enter the New England Deaconess Hospital for coma when it is not present. This is a fortunate error in diagnosis. We take great pains to encourage physicians to send patients into the hospital at once if in doubt about the question of coma and we train our patients to take no chances. Diabetic coma is confused with meningitis, septicemia, cerebral hemorrhage, uremia, an overdose of narcotics, and this is all the more apt to occur if the urine shows a Burgundy red color with ferric chlorid. But not all diabetics with Gerhard's reaction for diacetic acid are on the verge of coma, and, what is still more important, diacetic acid tests which are reported as positive frequently are simply erroneous tests caused by salicylic acid or its derivatives which give the same coloration. If the test for diacetic acid is a true one, on boiling the Burgundy red color disappears, but if false it remains unchanged.

The earliest and the best diagnostic symptom is the hyperpnea without cyanosis, and other symptoms are the soft eyeballs, dry skin, and rapid pulse. Pain in the abdomen or elsewhere, nausea, vomiting, and restlessness usually precede the coma itself.

Doctors' Emergency Insulin—With the diagnosis of diabetic coma once established either in the home or hospital treatment begins without delay. Frequently the physician gives insulin before the case is transferred to a hospital. In order that no time may be lost, whether the case is treated at home or in an institution, a precedent is being established in Massachusetts, through the aid of the John D. Rockefeller Junior Insulin Fund, by the distribution of Doctors' Emergency Insulin to each doctor in the state outside of Boston so that he will have a bottle in his bag. We believe in this way doctors unaccustomed to treating severe coma can gain experience with incipient coma, acquire confidence in the astounding efficacy of insulin, and, with much satisfaction to themselves, rescue many patients from death.

Treatment.—Insulin Dosage—The size of the first dose of

insulin in coma depends upon the doctor's estimate of the probable number of hours the patient can live without insulin. If the expectation of life is twenty-four hours, one would inject 20 units and repeat every hour until clinical improvement is evident or sugar in the urine or blood is clearly diminishing, if the expectation is twelve hours one would inject 40 units and repeat the dose in the same manner, changing the quantity to 20 units as the state of the patient warrants, but if the expectancy is only six hours one would inject 40 units every thirty minutes until improvement is manifest. Finally, in a case like our Case No 3021, who died three and a half hours after entrance today we would give 40 units of insulin every fifteen minutes. We never intend that a patient at the New England Deaconess Hospital shall come up to within two hours of death from coma without having received at least 150 units of insulin in the preceding hour.

Of our 31 cases to recover, the dosage of insulin varied between 20 units and 300 units in the first twenty-four hours. Case No 3877 recovered from her first attack of impending coma taking 30 units the first day, but in her second attack a few weeks later received 270 units. At the beginning of the second attack of coma she was given *outside* of the hospital the juice of 22 oranges! This was the patient whose pulse fell from 212 to 160 after gastric lavage. Case No 4279 received but 20 units of insulin the first day, but evidently needed more, because on the second day she was given 100 units. Case No 4271 came in twice in a precoma state with air hunger and a urine loaded with casts, yet he recovered with 25 units. It is because of these recoveries of certain cases with a small amount of insulin that we are conservative in its use and advise its administration in 20- or 40-unit doses at hourly, half-hourly, or quarter-hourly intervals. This keeps the doctor near the bedside, it is true, but in no other way do we believe that patients in diabetic coma will be saved.

The danger of hypoglycemia is slight with insulin given in the above manner. A single one of our cases had an insulin reaction, though the blood-sugar fell below normal on several occasions. So soon as the symptoms of coma lessen and the sugar in the urine and blood is nearing normal limits, the interval

between doses is increased and the size of the individual dose of insulin is decreased. One must be on the watch, however, for a relapse with a sudden rise of blood-sugar and a return of the coma state.

Insulin has been administered subcutaneously save on one or two occasions, and we find no reason to lead us to depart from this custom except in those cases with almost stagnant circulation as proved by a blood-pressure under 90 mm. mercury.

The first dose of insulin is the one which pays the greatest dividends. Remarkable improvement sometimes supervenes so quickly that one is thankful an heroic dose was not given at the start for fear the reaction might have been serious.

All the measures which diabetic patients are taught to put in practice at home when they feel ill or suspect coma were employed in the hospital.

Accessory Measures in Treatment—Without a special nurse a patient will get out of bed, will either take no nourishment or take it irregularly, will keep uncovered. Coma is a combat with death and the patient needs every help in the fight. Insulin has made the treatment more complicated, and all our friends treating coma in the various Boston hospitals agree that a doctor must be on hand to decide upon the next step. As yet one cannot write orders for a nurse to carry out for more than one or two hours for a patient in coma.

Warmth—Patient after patient with coma has entered the hospital with a rectal temperature below 96° F. It is common sense to conserve every atom of energy. Hence the urgency for keeping a patient warm from the inception of acidosis until recovery from it, whether in the ambulance or in the hospital.

Enema—Almost all patients with coma are constipated, and to protect the intestinal tract the bowels should be evacuated. Before the days of subcutaneous salt solution the chief dependence was upon the retention of saline enemata. For this a preliminary cleansing enema was necessary. For a like reason cathartics by mouth were avoided because of possible diarrhea. After six or eight hours it is often wise to repeat the enema.

Introduction of Liquids Into the Body—A coma patient is dry

When the coma is severe even the eyeballs are as soft as a jelly-fish. Obviously liquids must be supplied. It is liquid, not food, which the patient needs. Hot drinks are the best tolerated. It makes no particular difference what they are, save that if the patient gets broth, he gets salt solution, and if he gets coffee he gets a stimulant, and both are agreeable. Often one must contend with nausea. Strained water oatmeal gruel will suffice, but at times patients so yearn for orange juice that one must yield and give that. Milk is seldom as well tolerated. Hot water may be the final solution of the problem. Whatever the liquid one uses, one should always treat the patient as if he had just had a laparotomy, so gently, so carefully, should one administer it. To spare the stomach one gives salt solution or tap-water by the rectum. It is not desirable to give a patient in coma more than 20 grams of sodium chlorid in twenty-four hours, and in one's zeal to administer fluid this should not be forgotten.

The subpectoral injection of saline solution is of immense value, but it may not be an indifferent matter. A recent case of coma developed signs in the chest as described in the recent article by Kolodny,¹⁷ and it is possible that these were related to the subpectoral injection. So far as we are aware no similar symptoms have been observed in our other coma cases. x-Ray studies are necessary to exclude this possibility. It has been recommended that the salt solution be given in the thighs. This we have done, but without great success and with considerable pain to the patient. Perhaps with better technic our results would be better. We believe our success in treatment is closely connected with the free use we have made of subcutaneous injections of saline. With Case No 4232 we may have overdone the matter and produced renal block. She received 4 liters of salt solution subcutaneously and, in addition, saline by rectum. If more than 2 liters of fluid are indicated, we advise using plain water.

Intravenous infusion was employed in the pre-insulin cases, but not in the later series, but has been employed in 1 case since this article was written. It is too risky. Too sudden a

burden is thrown upon a weak heart, and furthermore it is difficult to carry out because of the low blood-pressure and small veins

Cardiac stimulation is essential. This is furnished by the warmth afforded the patient by heaters, by warm drinks by injection of salt solution, and, as for drugs, by caffeine. Often we give a coffee enema, and always caffeine subcutaneously in 5-grain doses every hour for the first few hours according to symptomatic needs. We have not given over 30 or 40 grains of caffeine in twenty-four hours.

The importance of *gastric lavage* we cannot assert too strongly. We have never regretted employing this agency and would refer to the discussion upon its advantages on pages 1225 and 1227.

Observations Desirable in Coma—No matter how complete we have believed the history and the laboratory data in any given case, when it comes to review much is found lacking. Especially needed is a better correlation between clinical and chemical findings in order to standardize treatment. All records of symptoms, signs, and therapeutic measures demand careful treatment as to time. If the general practitioner had a test for the stage of acidosis which he could use as easily as the routine tests for acidosis available in hospitals, more cases would be conquered. At present we hospital doctors and chemists, our laboratories afford really depend upon his ability to discover the coma case in its incipency.

Most of all in the treatment of diabetic coma is needed a simple test for the degree of acidosis which is practical and easy. The Gerhardt ferric chlorid test for carbon dioxide in blood,

History—The history of a case of coma often is of little value before admittance. Apparently very ill, with vomiting, such as vomiting, drowsiness, and "difficult breathing," may occur for hours or days at a time with temporary improvement before the patient finally comes to the hospital. Case No. 2627 illustrated this. During the week of November 17 to 19, 1922, she was constipated and had headaches. On November 19th nausea and vomiting with stupor and difficult breathing were present all day. Her doctor omitted fats and gave orange juice,

with improvement On November 23d an abscessed tooth was incised On November 27th nausea all day She entered the New England Deaconess Hospital at 10 P M November 27th with coma imminent The history must take account not only of patients' statements, but of the observations of parents, family, friends, and physician No history of coma is complete which does not begin with notes of the patient's condition at least one week before, including comments upon the diet and infractions of it, innocent or otherwise, the activity and hours of sleep of the patient, and upon the use or abuse of insulin

A full description of every case of coma is desirable, first to aid in the differential diagnosis, and second, to further our knowledge of diabetic coma, especially since insulin now has produced new and varied types of coma The following symptoms and signs need careful description They may be grouped under six main headings

1 General

(a) Headache frequently occurs in the prodromal stage Is it reflex from the constipation or a toxic effect? It is frequently a sharp pain over the eyes, shooting backward, and usually is overshadowed by other symptoms as the condition advances

(b) Pains in legs and arms Their explanation

(c) Loss of strength, an early warning of the insidious approach of coma

(d) Fever suggests a complication

2 Gastro-intestinal

(a) Loss of appetite requires explanation Is it a protective symptom?

(b) Nausea and vomiting What is their relation to acidosis? Their significance may vary at different stages Thus they may have a causal relationship in so far as dehydration is produced As a means of getting rid of harmful, excessive foods, they may be helpful In later stages with dilatation of the stomach patients apparently are unable to vomit and the contents are drooled from the mouth In general, a comatose patient has a better prognosis if he can vomit than if he cannot Case No 3240 had fecal material in the stomach even though her bowels

had moved freely Is there a toxic paralysis of the intestines with practical obstruction?

(c) Character and amount of vomitus, especially with reference to hemorrhage How important is the hemorrhage? Its association with leukocytosis

(d) Diarrhea with consequent dehydration

(e) Constipation

(f) Abdominal pain is a frequent puzzling and sometimes misleading symptom, varying in location and sometimes accompanied with marked muscle spasm Is this pain related to constipation, obstruction, dilatation of the stomach, or toxemia?

3 Neurologic

(a) Drowsiness seems related to the altered tissue chemistry Is the blood chemistry a satisfactory index? When does unconsciousness come about? What part is played by exhaustion? By toxic substances? By acidosis alone? Why do some patients continue long in a state of coma before death, while others die very shortly? A number of studies of the effects of exposure to CO_2 on the resistance of red cells to hemolysis by hypotonic salt solutions, etc , suggest that in coma high CO_2 in the tissues may affect the permeability of the cell membranes and so allow changed chemical relations with tissue fluids

(b) Reflex changes in coma Divergence of the eyes, dilatation of the pupils, absence of knee-jerks, loss of sphincteric control, inability to swallow, occur at different periods and inconstantly Blum in 1913 commented on the variability of these signs A comparison with modern chemical findings and the results of insulin treatment is needed

(c) What changes in chemistry occur in the fluids bathing the brain? The pressure and chemistry of the cerebrospinal fluid should be studied

4 Circulatory

(a) Pulse-rate, pulse-pressure, and variations in the character of the pulse

(b) Blood-pressure variations should be carefully watched, hour by hour Apparently the pressure falls as coma advances A systolic pressure below 100 is almost the rule, and if above 110

in an unconscious patient, raises the question of some other cause of the coma. When the systolic pressure is below 90 and the diastolic below 60, exhaustion is imminent. A stationary or a rising blood-pressure during the first few hours of treatment brightens the prognosis.

(c) Peripheral circulation. Cold hands and feet suggest slow blood flow and possibly capillary dilatation.

(d) Decreased blood volume together with concentration of the blood are interesting and important subjects for study.

(e) Cardiac function under the influence of change in blood volume and blood chemistry.

5 Respiratory

(a) Dyspnea, at first on exertion and then at rest. Air hunger with marked use of the accessory muscles varies in duration. Exhaustion brings on a shallow and feeble type of breathing. Rapidity of change from one type of breathing to another. Presence of Cheyne-Stokes or stertorous breathing is so uncommon as to suggest a complication.

(b) Stethoscopic evidence of early air hunger. Change in the physical signs of complicating pulmonary conditions in the presence of air hunger.

(c) Relation of the failure of the kidneys in coma to dyspnea.

(d) Great loss of water through the lungs due to the rapid respiration. This can be studied by simply measuring the rate of weight loss of the patient.

6 Renal. Studies upon renal efficiency before, at onset, during, and subsequent to coma.

Coma always has a cause. Search for that in order to treat cause as well as symptom.

Rules for Treatment of Diabetic Coma in Force at the New England Deaconess Hospital April, 1925 — Duties of Nurse —
A Preparations for Reception of Patient (1) A warm bed with blankets in place of sheets and at least 4 hot-water bags. (2) The necessary equipment in readiness at the bedside for catheterization, for a soap-suds enema, for gastric lavage, for subpectoral infusion of normal saline, for administration of caffeine and insulin.

B Care of Patient (1) Secure specimen of urine, by catheter if necessary. A specimen of urine is to be tested for sugar and diacetic acid every hour until recovery. If a self-retaining catheter is to be left in the bladder, urotropin (10 grains) should be given every four hours for three doses. (2) Hourly records of the pulse and two-hourly records of the respiration rate and temperature are to be kept. (3) Enema

Duties of Physician—A Examination of patient

B Constant attendance until the crisis is passed

C If diagnosis of coma is confirmed, write necessary orders for treatment with especial reference to (1) gastric lavage, (2) the method and rate of administration of liquids by mouth, rectum or subcutaneously. (3) the diet, (4) caffeine, and (5) insulin.

The purpose of gastric lavage is to prevent or relieve gastric dilatation.

Liquids by mouth must be given hot and at a rate not to exceed 100 cc. an hour. Liquids by rectum, salt solution, black coffee, or tepid water may be given every two hours for two doses and thereafter every four hours. If the patient is dry unhesitatingly give salt solution subcutaneously. In the presence of primary diabetes the skin may be dry and the skin of the thighs. If the temperature rises to 101° F. or above give very slowly 250 to 500 cc. and as soon as the temperature has elapsed. One cc. of solution from a 100 cc. ampoule may be added to the salt solution when the patient is very thirsty. Do not give below 90°

The diet should not contain more than 50 grams of protein 25 grams and fat 25 grams in 24 hours unless vomiting by nausea or other means. This is represented by 2 small oranges or 1 small apple equivalent to 500 grams of milk. Give 100 cc. of orange juice (the juice of two small oranges) or 100 cc. of apple juice or cream 100 cc. Brown coffee or black coffee or tea as vehicles for the above.

Caffeine sodium benzoate is a potent stimulant and should be given every hour for 100 cc. of orange juice or 100 cc. of apple juice.

The gravity of the coma is evidenced by the degree of stupor, the exhaustion of the patient as shown by a rectal temperature of 95° F or below, by circulatory collapse with blood-pressure below 80 systolic, dry mucous membranes and skin, soft eyeballs, and by hemorrhagic vomitus or gastric contents. Air hunger if slight but definite at first, increases to a maximum, and toward the end gives way to shallow respiration.

The size of the first dose of insulin in coma depends upon the doctor's estimation of the probable number of hours the patient can live without insulin. If the patient's expectation of life is twenty-four hours, one would inject 20 units and repeat every hour until clinical improvement and sugar in the urine or blood is approaching normal, if the patient's expectation is twelve hours one would inject 40 units and repeat the dose in the same manner, changing the quantity to 20 units as the state of the patient warrants, but if the expectation is only six hours, one would inject 40 units every thirty minutes until improvement is manifest. Finally, in a case like our Case No. 3021, who died three and a half hours after entrance, we should now give 40 units of insulin every fifteen minutes. We never intend to have a patient at the New England Deaconess Hospital come up to within two hours of death from coma without having received at least 150 units of insulin in the preceding hour.

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CLINIC OF DRS ELLIOTT P JOSLIN HOWARD F
ROOT PRISCILLA WHITE, AND EVERETT D KIEFER¹

NEW ENGLAND DEACONESS HOSPITAL

A DEATH FROM DIABETIC COMA AND WHY

BETWEEN January 1, 1923 and April 1, 1925 33 patients in diabetic coma have been admitted to the New England Deaconess Hospital and 2 have died. A death from coma, therefore, is so unusual that one must investigate why it occurs. The present case is particularly appropriate to bring before you because it illustrates and emphasizes so many of the points discussed at our recent conference on diabetic coma, and because one of your own number stayed up the greater part of the night for the chemical investigation of the blood and urine.

Here is the pathetic story. Mrs. G., whose diabetes was discovered in March, 1923 because of a boil on her leg, never followed her diet closely, but had taken insulin, three doses daily amounting to a total of 20 units, until January, 1925. Diet was then given up, insulin omitted, and thus two cardinal principles in the treatment of diabetes violated.

A diabetic patient can break his diet and live for days or even years, depending upon the severity of his disease. But a diabetic patient who breaks his diet and gives up insulin, you can be very sure is not long for this world.

If the supply of insulin fails the diabetic patient should reduce his diet one-third, or even more if his diet has been increased more than one-third above what he could tolerate without insulin. At the three lectures we doctors give and the three talks the nurses give weekly to the patients at the hospital we endeavor

¹ Everybody works over a case of diabetic coma, and the youngest works the hardest. So we all four present this clinic.

to impress this upon all who are taking insulin, and before they leave the hospital give them these instructions in writing. On the other hand when food is omitted for one reason or another, it is not so generally understood what the patient is to do about his insulin. A safe rule for him under these circumstances is to reduce it also one-third, and if he is worried about a reaction every dose of insulin can be halved, and instead of taking the insulin three times a day he can take this small dose six times a day, $1\frac{1}{2}$, every four hours. The patient should realize that carbohydrate is being formed out of body protein, even though he takes no food. Thus was the advice given to the patient who reported by radiogram from the mid-Atlantic that he was seasick and taking no food and asked what he should do about insulin. Diabetic patients always eat—if they do not get food at their meal hours, they eat their own bodies at all hours, and therefore one must give insulin accordingly. But now let us seek for additional causes for coma and possible causes for death.

Infections appear to have clung to this patient. Her diabetes began, or at least was discovered, because of a boil on her leg. She developed an abscess on her thumb in November, 1921. Perhaps this accounted for the abscesses on each thigh in January, 1925, about the time she gave up insulin. In February there was an abscess on the labia, which healed more or less, but another labial abscess began on April 6th, broke on April 12th, and had become a large carbuncle when she entered the hospital on April 17th. This was the third cause for coma: first, breaking diet, second, giving up insulin, and third, an infection. One could predict that coma would soon supervene with this triad for premises.

The symptomatology of the onset of the coma is typical. Note the sequence: Diet and insulin given up in January, local abscess in February, on April 13th a carbuncle and the patient takes to bed with headaches and nervousness. On April 15th thirst is extreme and she drinks copiously. Nausea and vomiting follow. At 4 P.M. the next afternoon, April 16th, the day before admission, her husband notices that she is in a drowsy, dazed condition, and apparently does not see well. By 9 o'clock in

the evening respiration is labored and a doctor is called at 10, who gives pills. Nausea continues through the night and without result she tries to vomit. By 2 A M on April 17th Mrs G is unable to respond intelligently although questions are understood.

These then are the typical symptoms—drowsiness verging on coma, Kussmaul respiration, nausea and vomiting. Often there is pain, and this patient had headaches a few days before, but a not uncommon site of pain is in the abdomen and leads to confusion with appendicitis, gall-stone colic, and perforated duodenal ulcer. Often the pain is in the chest and pneumonia is simulated, though at times it actually exists and is the activating, infectious agent in the cause of coma, just as the abscesses were in this patient.

Between 2 A M, when drowsiness began, and 2 50 P M the same day, April 17th, the story of the patient is more or less a blank, but the story which was given by the physician of his attempts to get the patient into a hospital is vivid and tragic. Two large hospitals refused admission to this woman in diabetic coma because their beds were full. Do you believe that if this patient had had acute fulminating appendicitis she would have been refused, or if the doctor's diagnosis had been a perforated duodenal ulcer, that she would have been refused? What justification is there for refusing an emergency like a case of diabetic coma? Already you have heard that 31 out of our 33 cases of diabetic coma recovered. What hospital can show a record of 31 out of 33 cases of fulminating appendicitis or of perforated duodenal ulcer who recover? If a hospital is to save life why should it not try to save it? What hospital with a capacity of 300 or 400 beds would dare to face the community, when asking for funds, and say they would refuse an emergency case of appendicitis or of duodenal ulcer? It is time superintendents of hospitals realized that diabetic coma is a curable emergency—just the sort of emergency a hospital is intended to treat.

The prevalent attitude of large general hospitals toward the diabetic is wrong in three ways—first, diabetic coma is an emer-

gency and is a diagnosis which merits admission, and yet it is not treated as such. Second, diabetic patients are seldom grouped in hospitals, but are scattered through the wards, with the result that any systematic attempt at teaching or treating them is rendered futile because it becomes so expensive and so individualistic. Diabetics should be kept closely together so that they can be treated economically. Third, the hospital stay of diabetics is too long. At the New England Deaconess Hospital we make one bed serve for 3 patients every month, in other words, our hospital stay is ten days. We are able to do so because of the intensive teaching of the patients. The teaching is cheaper than hospital board. Of course it means additional work for the doctors and for the nurses who must change the diet daily, but it pays because the patients are not hospitalized and can save their money, and it enables us to extend our influence over a wide clientèle.

The patient arrived at the hospital cold, dry, slightly cyanotic, pulseless, but mark you, she was able to give her name. Her eyeballs were soft and slightly diverging, and the nose appeared as if bloody vomitus had been expelled through it. The apex of the heart could not be seen or felt and sounds could only be detected in a small area. Respiration was of the Kussmaul type. There was no evidence of tenderness or spasm in the abdomen. Locally there was a large indurated carbuncle of the left labia the size of a lemon and with a slight discharge.

In anticipation of the arrival of the patient there were assembled a warm bed with blankets and 4 hot-water bottles, a catheter, a stomach-tube, a rectal tube, salt solution ready for subcutaneous use, and syringes filled with insulin and caffeine sodiobenzoate. Time counts in a case of coma, but in one's zeal for treatment one must never neglect a careful diagnosis.

The rectal temperature was 91° F.

The urine showed 3 per cent of sugar. Coma cases, as H F Root has pointed out nearly always show small percentages of sugar. The diacetic acid was 1+. In our last case sent in for coma the ferric chlorid test was 4+, but it was not due to diacetic acid and this the doctor overlooked. The Burgundy

red color with ferric chlorid always disappears by boiling if it is caused by diacetic acid, but persists in spite of boiling if caused by one of the salicylic acid preparations

How much insulin should we give the patient? Our present rule is an easy one to follow. If the probable expectation of life of the coma patient without insulin is twenty-four hours, one gives 20 units every hour, if the expectation is but twelve hours, one gives 40 units every hour, if the expectation is six hours, one gives 40 units every thirty minutes, and if one thinks it likely that the patient will not survive three hours, one gives 40 units every fifteen minutes, or at any rate sees to it that the patient receives 150 units of insulin at least in the third hour preceding his probable death without insulin. This patient received in her first five hours in the hospital 477 units, of which 332 units were given intravenously. With such a degree of capillary stasis present as was indicated by the lack of bleeding from the operative incision, the chance of getting insulin to the tissues most in need of it seems better if it is given intravenously than if given subcutaneously. As a rule in coma we have given insulin subcutaneously.

That severe infections of this sort may interfere with the utilization of insulin by the tissues is suggested by the fact that such large doses of insulin were required to produce but a moderate change in blood chemistry. None of the insulin given could have been lost in the urine, since none was passed after 6 p. m., and possibly renal activity had ceased earlier.

So soon as possible after admission an enema was given, the stomach proved by lavage to be empty, salt solution 1000 c.c. given subpectorally, and caffeine sodiobenzoate administered in $7\frac{1}{2}$ -grain doses about every hour until the patient had received 35 grains. A blood-culture was taken, and two hours after admission the carbuncle was opened without anesthesia and without recognition of the event on the part of the patient.

The bladder contained at least 900 c.c. of urine, and later 150 c.c. were obtained, and two hours later 120 c.c. The percentage of sugar did not change more than 0.1 per cent in all three specimens, thus raising the query as to whether a

gency and is a diagnosis which merits admission, and yet it is not treated as such. Second, diabetic patients are seldom grouped in hospitals, but are scattered through the wards with the result that any systematic attempt at teaching or treating them is rendered futile because it becomes so expensive and so individualistic. Diabetics should be kept closely together so that they can be treated economically. Third, the hospital stay of diabetics is too long. At the New England Deaconess Hospital we make one bed serve for 3 patients every month, in other words, our hospital stay is ten days. We are able to do so because of the intensive teaching of the patients. The teaching is cheaper than hospital board. Of course it means additional work for the doctors and for the nurses who must change the diet daily, but it pays because the patients are not hospitalized and can save their money, and it enables us to extend our influence over a wide clientèle.

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urine at all was being secreted. This may or may not account for the fact that there was no evidence of excretion of phenolphthalein in two hours after this was injected. So often are the kidneys affected in coma that we sought this means of testing their efficiency. The urine sediment was loaded as usual with granular casts.

Absolute correlation between clinical and chemical findings in coma does not exist. The carbon dioxide combining power of the blood plasma in this patient at admission was below the scale and was estimated at 5 volumes per cent. An hour later it was the same, but in the next hour it rose to 8 volumes per cent. Between 7 and 11 P. M. it varied between 14 and 13 in four observations. Here, then, is a patient in diabetic coma who can give her name, but whose blood has a CO_2 combining power at 5. Usually patients are unconscious when the CO_2 combining power is about 14 volumes per cent, but we have seen other cases at the hospital where the patient could be roused when the combining power was as low as 7 volumes per cent.

The CO_2 combining power rose from below the scale to 14 volumes per cent without alkalis, but with insulin. Alkalis were given up at our hospital in 1916 and 1917, and it is a satisfaction that our clinical judgment has been chemically confirmed by Haldane in Cambridge, England, during the last few months. He has shown that sodium bicarbonate in sufficient doses, when given to a normal person, will provoke the excretion of acetone in the urine, and he furthermore definitely ascribes to sodium bicarbonate the responsibility for producing his low respiratory quotient of 0.64 because of its interference with the normal carbohydrate metabolism.

The percentage of sugar in the blood also established a record for the hospital, but not for our patients outside the hospital, with one of whom it was 1.37 per cent. At entrance it was 0.80 per cent, in the next hour 0.78 per cent, but at 5 P. M. 0.90 per cent, at 6 P. M. 0.89 per cent, and this after nearly 300 units of insulin. At this stage it began to fall, and in the next two hours was 0.70 per cent, in the next hour 0.62 per cent, and at 11 P. M.

of her eyeballs was better and recovery seemed not unlikely, especially because of the falling blood-sugar and the fact that she had taken a little liquid. Two hours later she began to be a little delirious and talked incoherently. She did not respond to questions and in this condition she remained until a few minutes before death at 2 40 A M.

Post-mortem examination was granted. In the abdomen there was found a beginning general peritonitis which probably had had its origin in the blood-stream rather than by direct extension from the carbuncle. The kidneys showed grossly an acute glomerulonephritis. The blood-culture taken upon admission was reported at the end of seventy-two hours positive with staphylococci, and staphylococci were found in the smear taken from the carbuncle.

The patient died in diabetic coma and must be classed in our records as a diabetic coma death. If life had been prolonged a few hours, presumably she would have suffered a death from general peritonitis or failing that, from septicemia.

A diabetic breaks diet, gives up insulin, and develops local infections. One of these forces her to bed. Intense thirst is followed by copious drinking of liquids, and in turn by nausea and vomiting, drowsiness, and deep breathing. She becomes unconscious at 2 A M but reaches the hospital twelve hours later and gives her name, though the CO_2 combining power in her blood is 5 volumes per cent. Yet with subcutaneous salt solution, caffeine, and 497 units of insulin her CO_2 rises to 14 volumes per cent, and her blood-sugar percentage is lowered from 0.90 to 0.44 per cent. She even takes liquids by the mouth, but the blood-pressure never rises above 72 millimeters mercury systolic. Kussmaul respiration is replaced by the feeble breathing of exhaustion and after a period of listless delirium she dies. The blood-culture taken upon admission is positive for staphylococci, and these are also found in a carbuncle of the labia. There is a beginning general peritonitis.

Another needless death from diabetic coma

and 1 A M it was 0.54 each time, and a few minutes before death, at 2.40 it was 0.44

Under the influence of insulin, salt solution under the skin, and a little (300 c c) intravenously, and black coffee by rectum, the patient roused up toward 5.30 P M sufficiently to be able to take by mouth nearly 300 c c of water and broth in teaspoonful doses. By 8 P M the Kussmaul respiration had disappeared and was replaced by breathing so feeble that we hung the blankets over the bed to take their weight off her chest.

Pulseless at first, the pulse gradually improved up to within a few minutes of death.

The blood-pressure was first taken one-half hour after entrance and was then 60/40. An hour later it had risen to 70 systolic and still later to 72. The blood-pressure is one of the most valuable adjuncts for prognosis of diabetic coma cases. Only 1 of our coma patients had a blood-pressure as low as 70 systolic and recovered.

As a matter of record several other observations may be noted. The hemoglobin was 60 per cent. The red blood-count was 6,208,000, undoubtedly due to the concentration of the blood. The white blood-count was 28,000, and in this case can readily be explained by the abscess. In other cases, as we have pointed out elsewhere, the white blood-count may be as high, but due to a gastric hemorrhage which is not at all uncommon in coma. The blood calcium was 10.5 milligrams per 100 c c. The bilirubin was 0.7 milligram per 100 c c. The plasma salt was 565 milligrams. The non-protein nitrogen in coma is always high, and in 1 of our patients on the third day of coma rose to 100 milligrams, and on the next day to 138 milligrams, and yet the young girl recovered. In this case the non-protein nitrogen was 16 milligrams at entrance and at 5, 6, and 7 P M it was 68, 72, and 85 milligrams respectively. A few hours before death, at two observations, it was 58 and 63 milligrams.

The state of the patient changed at 8 o'clock, six hours after entrance, when the respiration became shallow and the patient gave the impression that she was simply dozing, worn out with her strenuous days of air hunger. Her color was good, the tension

of her eyeballs was better, and recovery seemed not unlikely, especially because of the falling blood-sugar and the fact that she had taken a little liquid. Two hours later she began to be a little delirious and talked incoherently. She did not respond to questions and in this condition she remained until a few minutes before death at 2 40 A M.

Post-mortem examination was granted. In the abdomen there was found a beginning general peritonitis which probably had had its origin in the blood-stream rather than by direct extension from the carbuncle. The kidneys showed grossly an acute glomerulonephritis. The blood-culture taken upon admission was reported at the end of seventy-two hours positive with staphylococci, and staphylococci were found in the smear taken from the carbuncle.

The patient died in diabetic coma and must be classed in our records as a diabetic coma death. If life had been prolonged a few hours, presumably she would have suffered a death from general peritonitis or, failing that, from septicemia.

A diabetic breaks diet, gives up insulin, and develops local infections. One of these forces her to bed, intense thirst is followed by copious drinking of liquids, and in turn by nausea and vomiting, drowsiness, and deep breathing. She becomes unconscious at 2 A M but reaches the hospital twelve hours later and gives her name, though the CO_2 combining power in her blood is 5 volumes per cent. Yet with subcutaneous salt solution, caffeine, and 497 units of insulin her CO_2 rises to 14 volumes per cent, and her blood-sugar percentage is lowered from 0.90 to 0.44 per cent. She even takes liquids by the mouth, but the blood-pressure never rises above 72 millimeters mercury systolic. Kussmaul respiration is replaced by the feeble breathing of exhaustion, and after a period of listless delirium she dies. The blood-culture taken upon admission is positive for staphylococci, and these are also found in a carbuncle of the labia. There is a beginning general peritonitis.

Another needless death from diabetic coma

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